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(54) Title: NOVEL NUCLEIC ACIDS AND POLYPEPTIDES

(57) Abstract: The present invention provides novel nucleic acids, novel polypeptide sequences encoded by these nucleic acids and uses thereof.

NOVEL NUCLEIC ACIDS AND POLYPEPTIDES

1. TECHNICAL FIELD

The present invention provides novel polynucleotides and proteins encoded by such polynucleotides, along with uses for these polynucleotides and proteins, for example in therapeutic, diagnostic and research methods.

2. BACKGROUND

Technology aimed at the discovery of protein factors (including *e.g.*, cytokines, such as lymphokines, interferons, CSFs, chemokines, and interleukins) has matured rapidly over the past decade. The now routine hybridization cloning and expression cloning techniques clone novel polynucleotides "directly" in the sense that they rely on information directly related to the discovered protein (*i.e.*, partial DNA/amino acid sequence of the protein in the case of hybridization cloning; activity of the protein in the case of expression cloning). More recent "indirect" cloning techniques such as signal sequence cloning, which isolates DNA sequences based on the presence of a now well-recognized secretory leader sequence motif, as well as various PCR-based or low stringency hybridization-based cloning techniques, have advanced the state of the art by making available large numbers of DNA/amino acid sequences for proteins that are known to have biological activity, for example, by virtue of their secreted nature in the case of leader sequence cloning, by virtue of their cell or tissue source in the case of PCR-based techniques, or by virtue of structural similarity to other genes of known biological activity.

Identified polynucleotide and polypeptide sequences have numerous applications in, for example, diagnostics, forensics, gene mapping; identification of mutations responsible for genetic disorders or other traits, to assess biodiversity, and to produce many other types of data and products dependent on DNA and amino acid sequences.

3. SUMMARY OF THE INVENTION

The compositions of the present invention include novel isolated polypeptides, novel isolated polynucleotides encoding such polypeptides, including recombinant DNA molecules, cloned genes or degenerate variants thereof, especially naturally occurring variants such as allelic variants, antisense polynucleotide molecules, and antibodies that specifically recognize one or more epitopes present on such polypeptides, as well as hybridomas producing such antibodies.

The compositions of the present invention additionally include vectors, including expression vectors, containing the polynucleotides of the invention, cells genetically engineered to contain such polynucleotides and cells genetically engineered to express such polynucleotides.

The present invention relates to a collection or library of at least one novel nucleic acid sequence assembled from expressed sequence tags (ESTs) isolated mainly by sequencing by hybridization (SBH), and in some cases, sequences obtained from one or more public databases. The invention relates also to the proteins encoded by such polynucleotides, along with therapeutic, diagnostic and research utilities for these polynucleotides and proteins. These nucleic acid sequences are designated as SEQ ID NO: 1-30368. The polypeptides sequences are designated SEQ ID NO: 30369-60736. The nucleic acids and polypeptides are provided in the Sequence Listing. In the nucleic acids provided in the Sequence Listing, A is adenosine; C is cytosine; G is guanine; T is thymine; and N is any of the four bases. In the amino acids provided in the Sequence Listing, * corresponds to the stop codon.

The nucleic acid sequences of the present invention also include, nucleic acid sequences that hybridize to the complement of SEQ ID NO: 1-30368 under stringent hybridization conditions; nucleic acid sequences which are allelic variants or species homologues of any of the nucleic acid sequences recited above, or nucleic acid sequences that encode a peptide comprising a specific domain or truncation of the peptides encoded by SEQ ID NO: 1-30368. A polynucleotide comprising a nucleotide sequence having at least 90% identity to an identifying sequence of SEQ ID NO: 1-30368 or a degenerate variant or fragment thereof. The identifying sequence can be 100 base pairs in length.

The nucleic acid sequences of the present invention also include the sequence information from the nucleic acid sequences of SEQ ID NO: 1-30368. The sequence information can be a segment of any one of SEQ ID NO: 1-30368 that uniquely identifies or represents the sequence information of SEQ ID NO: 1-30368.

A collection as used in this application can be a collection of only one polynucleotide. The collection of sequence information or identifying information of each sequence can be provided on a nucleic acid array. In one embodiment, segments of sequence information is provided on a nucleic acid array to detect the polynucleotide that contains the segment. The array can be designed to detect full-match or mismatch to the polynucleotide that contains the segment. The collection can also be provided in a computer-readable format.

This invention also includes the reverse or direct complement of any of the nucleic acid sequences recited above; cloning or expression vectors containing the nucleic acid sequences; and host cells or organisms transformed with these expression vectors. Nucleic acid sequences (or their reverse or direct complements) according to the invention have numerous applications in a variety of techniques known to those skilled in the art of molecular biology, such as use as hybridization probes, use as primers for PCR, use in an array, use in computer-readable media, use in sequencing

full-length genes, use for chromosome and gene mapping, use in the recombinant production of protein, and use in the generation of anti-sense DNA or RNA, their chemical analogs and the like.

In a preferred embodiment, the nucleic acid sequences of SEQ ID NO: 1-30368 or novel segments or parts of the nucleic acids of the invention are used as primers in expression assays that are well known in the art. In a particularly preferred embodiment, the nucleic acid sequences of SEQ ID NO: 1-30368 or novel segments or parts of the nucleic acids provided herein are used in diagnostics for identifying expressed genes or, as well known in the art and exemplified by Vollrath et al., Science 258:52-59 (1992), as expressed sequence tags for physical mapping of the human genome.

The isolated polynucleotides of the invention include, but are not limited to, a polynucleotide comprising any one of the nucleotide sequences set forth in SEQ ID NO: 1-30368; a polynucleotide comprising any of the full length protein coding sequences of SEQ ID NO: 1-30368; and a polynucleotide comprising any of the nucleotide sequences of the mature protein coding sequences of SEQ ID NO: 1-30368. The polynucleotides of the present invention also include, but are not limited to, a polynucleotide that hybridizes under stringent hybridization conditions to (a) the complement of any one of the nucleotide sequences set forth in SEQ ID NO: 1-30368; (b) a nucleotide sequence encoding any one of the amino acid sequences set forth in the Sequence Listing (*e.g.*, SEQ ID NO: 30369-60736); (c) a polynucleotide which is an allelic variant of any polynucleotides recited above; (d) a polynucleotide which encodes a species homolog (*e.g.* orthologs) of any of the proteins recited above; or (e) a polynucleotide that encodes a polypeptide comprising a specific domain or truncation of any of the polypeptides comprising an amino acid sequence set forth in the Sequence Listing.

The isolated polypeptides of the invention include, but are not limited to, a polypeptide comprising any of the amino acid sequences set forth in the Sequence Listing; or the corresponding full length or mature protein. Polypeptides of the invention also include polypeptides with biological activity that are encoded by (a) any of the polynucleotides having a nucleotide sequence set forth in SEQ ID NO: 1-30368; or (b) polynucleotides that hybridize to the complement of the polynucleotides of (a) under stringent hybridization conditions. Biologically or immunologically active variants of any of the polypeptide sequences in the Sequence Listing, and "substantial equivalents" thereof (*e.g.*, with at least about 65%, 70%, 75%, 80%, 85%, 90%, 95%, 98% or 99% amino acid sequence identity) that preferably retain biological activity are also contemplated. The polypeptides of the invention may be wholly or partially chemically synthesized but are preferably produced by recombinant means using the genetically engineered cells (*e.g.* host cells) of the invention.

The invention also provides compositions comprising a polypeptide of the invention. Polypeptide compositions of the invention may further comprise an acceptable carrier, such as a hydrophilic, *e.g.*, pharmaceutically acceptable, carrier.

The invention also provides host cells transformed or transfected with a polynucleotide of the invention.

The invention also relates to methods for producing a polypeptide of the invention comprising growing a culture of the host cells of the invention in a suitable culture medium under conditions permitting expression of the desired polypeptide, and purifying the polypeptide from the culture or from the host cells. Preferred embodiments include those in which the protein produced by such process is a mature form of the protein.

Polynucleotides according to the invention have numerous applications in a variety of techniques known to those skilled in the art of molecular biology. These techniques include use as hybridization probes, use as oligomers, or primers, for PCR, use for chromosome and gene mapping, use in the recombinant production of protein, and use in generation of anti-sense DNA or RNA, their chemical analogs and the like. For example, when the expression of an mRNA is largely restricted to a particular cell or tissue type, polynucleotides of the invention can be used as hybridization probes to detect the presence of the particular cell or tissue mRNA in a sample using, *e.g., in situ* hybridization.

In other exemplary embodiments, the polynucleotides are used in diagnostics as expressed sequence tags for identifying expressed genes or, as well known in the art and exemplified by Vollrath et al., Science 258:52-59 (1992), as expressed sequence tags for physical mapping of the human genome.

The polypeptides according to the invention can be used in a variety of conventional procedures and methods that are currently applied to other proteins. For example, a polypeptide of the invention can be used to generate an antibody that specifically binds the polypeptide. Such antibodies, particularly monoclonal antibodies, are useful for detecting or quantitating the polypeptide in tissue. The polypeptides of the invention can also be used as molecular weight markers, and as a food supplement.

Methods are also provided for preventing, treating, or ameliorating a medical condition which comprises the step of administering to a mammalian subject a therapeutically effective amount of a composition comprising a polypeptide of the present invention and a pharmaceutically acceptable carrier.

In particular, the polypeptides and polynucleotides of the invention can be utilized, for example, in methods for the prevention and/or treatment of disorders involving aberrant protein expression or biological activity.

The present invention further relates to methods for detecting the presence of the polynucleotides or polypeptides of the invention in a sample. Such methods can, for example, be utilized as part of prognostic and diagnostic evaluation of disorders as recited herein and for the identification of subjects exhibiting a predisposition to such conditions. The invention provides a method for detecting the polynucleotides of the invention in a sample, comprising contacting the sample with a compound that binds to and forms a complex with the polynucleotide of interest for a period sufficient to form the complex and under conditions sufficient to form a complex and detecting the complex such that if a complex is detected, the polynucleotide of interest is detected. The invention also provides a method for detecting the polypeptides of the invention in a sample comprising contacting the sample with a compound that binds to and forms a complex with the polypeptide under conditions and for a period sufficient to form the complex and detecting the formation of the complex such that if a complex is formed, the polypeptide is detected.

The invention also provides kits comprising polynucleotide probes and/or monoclonal antibodies, and optionally quantitative standards, for carrying out methods of the invention. Furthermore, the invention provides methods for evaluating the efficacy of drugs, and monitoring the progress of patients, involved in clinical trials for the treatment of disorders as recited above.

The invention also provides methods for the identification of compounds that modulate (*i.e.*, increase or decrease) the expression or activity of the polynucleotides and/or polypeptides of the invention. Such methods can be utilized, for example, for the identification of compounds that can ameliorate symptoms of disorders as recited herein. Such methods can include, but are not limited to, assays for identifying compounds and other substances that interact with (*e.g.*, bind to) the polypeptides of the invention. The invention provides a method for identifying a compound that binds to the polypeptides of the invention comprising contacting the compound with a polypeptide of the invention in a cell for a time sufficient to form a polypeptide/compound complex, wherein the complex drives expression of a reporter gene sequence in the cell; and detecting the complex by detecting the reporter gene sequence expression such that if expression of the reporter gene is detected the compound that binds to a polypeptide of the invention is identified.

The methods of the invention also provides methods for treatment which involve the administration of the polynucleotides or polypeptides of the invention to individuals exhibiting symptoms or tendencies. In addition, the invention encompasses methods for treating diseases or disorders as recited herein comprising administering compounds and other substances that modulate the overall activity of the target gene products. Compounds and other substances can

effect such modulation either on the level of target gene/protein expression or target protein activity.

The polypeptides of the present invention and the polynucleotides encoding them are also useful for the same functions known to one of skill in the art as the polypeptides and polynucleotides to which they have homology (set forth in the sequence listing). If no homology is set forth for a sequence, then the polypeptides and polynucleotides of the present invention are useful for a variety of applications, as described herein, including use in arrays for detection.

4. DETAILED DESCRIPTION OF THE INVENTION

4.1 DEFINITIONS

It must be noted that as used herein and in the appended claims, the singular forms "a", "an" and "the" include plural references unless the context clearly dictates otherwise.

The term "active" refers to those forms of the polypeptide which retain the biologic and/or immunologic activities of any naturally occurring polypeptide. According to the invention, the terms "biologically active" or "biological activity" refer to a protein or peptide having structural, regulatory or biochemical functions of a naturally occurring molecule. Likewise "immunologically active" or "immunological activity" refers to the capability of the natural, recombinant or synthetic polypeptide to induce a specific immune response in appropriate animals or cells and to bind with specific antibodies.

The term "activated cells" as used in this application are those cells which are engaged in extracellular or intracellular membrane trafficking, including the export of secretory or enzymatic molecules as part of a normal or disease process.

The terms "complementary" or "complementarity" refer to the natural binding of polynucleotides by base pairing. For example, the sequence 5'-AGT-3' binds to the complementary sequence 3'-TCA-5'. Complementarity between two single-stranded molecules may be "partial" such that only some of the nucleic acids bind or it may be "complete" such that total complementarity exists between the single stranded molecules. The degree of complementarity between the nucleic acid strands has significant effects on the efficiency and strength of the hybridization between the nucleic acid strands.

The term "embryonic stem cells (ES)" refers to a cell that can give rise to many differentiated cell types in an embryo or an adult, including the germ cells. The term "germ line stem cells (GSCs)" refers to stem cells derived from primordial stem cells that provide a steady and continuous source of germ cells for the production of gametes. The term "primordial germ

cells (PGCs)" refers to a small population of cells set aside from other cell lineages particularly from the yolk sac, mesenteries, or gonadal ridges during embryogenesis that have the potential to differentiate into germ cells and other cells. PGCs are the source from which GSCs and ES cells are derived The PGCs, the GSCs and the ES cells are capable of self-renewal. Thus these cells not only populate the germ line and give rise to a plurality of terminally differentiated cells that comprise the adult specialized organs, but are able to regenerate themselves.

The term "expression modulating fragment," EMF, means a series of nucleotides which modulates the expression of an operably linked ORF or another EMF.

As used herein, a sequence is said to "modulate the expression of an operably linked sequence" when the expression of the sequence is altered by the presence of the EMF. EMFs include, but are not limited to, promoters, and promoter modulating sequences (inducible elements). One class of EMFs are nucleic acid fragments which induce the expression of an operably linked ORF in response to a specific regulatory factor or physiological event.

The terms "nucleotide sequence" or "nucleic acid" or "polynucleotide" or "oligonucleotide" are used interchangeably and refer to a heteropolymer of nucleotides or the sequence of these nucleotides. These phrases also refer to DNA or RNA of genomic or synthetic origin which may be single-stranded or double-stranded and may represent the sense or the antisense strand, to peptide nucleic acid (PNA) or to any DNA-like or RNA-like material. In the sequences herein A is adenine, C is cytosine, T is thymine, G is guanine and N is A, C, G or T (U). It is contemplated that where the polynucleotide is RNA, the T (thymine) in the sequences provided herein is substituted with U (uracil). Generally, nucleic acid segments provided by this invention may be assembled from fragments of the genome and short oligonucleotide linkers, or from a series of oligonucleotides, or from individual nucleotides, to provide a synthetic nucleic acid which is capable of being expressed in a recombinant transcriptional unit comprising regulatory elements derived from a microbial or viral operon, or a eukaryotic gene.

The terms "oligonucleotide fragment" or a "polynucleotide fragment", "portion," or "segment" or "probe" or "primer" are used interchangeably and refer to a sequence of nucleotide residues which are at least about 5 nucleotides, more preferably at least about 7 nucleotides, more preferably at least about 9 nucleotides, more preferably at least about 11 nucleotides and most preferably at least about 17 nucleotides. The fragment is preferably less than about 500 nucleotides, preferably less than about 200 nucleotides, more preferably less than about 100 nucleotides, more preferably less than about 50 nucleotides and most preferably less than 30 nucleotides. Preferably the probe is from about 6 nucleotides to about 200 nucleotides, preferably from about 15 to about 50 nucleotides, more preferably from about 17 to 30 nucleotides and most preferably from about 20 to 25 nucleotides. Preferably the fragments can

be used in polymerase chain reaction (PCR), various hybridization procedures or microarray procedures to identify or amplify identical or related parts of mRNA or DNA molecules. A fragment or segment may uniquely identify each polynucleotide sequence of the present invention. Preferably the fragment comprises a sequence substantially similar to any one of SEQ ID NO: 1-30368.

Probes may, for example, be used to determine whether specific mRNA molecules are present in a cell or tissue or to isolate similar nucleic acid sequences from chromosomal DNA as described by Walsh et al. (Walsh, P.S. et al., 1992, PCR Methods Appl 1:241-250). They may be labeled by nick translation, Klenow fill-in reaction, PCR, or other methods well known in the art. Probes of the present invention, their preparation and/or labeling are elaborated in Sambrook, J. et al., 1989, Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, NY; or Ausubel, F.M. et al., 1989, Current Protocols in Molecular Biology, John Wiley & Sons, New York NY, both of which are incorporated herein by reference in their entirety.

The nucleic acid sequences of the present invention also include the sequence information from the nucleic acid sequences of SEQ ID NO: 1-30368. The sequence information can be a segment of any one of SEQ ID NO: 1-30368 that uniquely identifies or represents the sequence information of that sequence of SEQ ID NO: 1-30368. One such segment can be a twenty-mer nucleic acid sequence because the probability that a twenty-mer is fully matched in the human genome is 1 in 300. In the human genome, there are three billion base pairs in one set of chromosomes. Because 4^{20} possible twenty-mers exist, there are 300 times more twenty-mers than there are base pairs in a set of human chromosomes. Using the same analysis, the probability for a seventeen-mer to be fully matched in the human genome is approximately 1 in 5. When these segments are used in arrays for expression studies, fifteen-mer segments can be used. The probability that the fifteen-mer is fully matched in the expressed sequences is also approximately one in five because expressed sequences comprise less than approximately 5% of the entire genome sequence.

Similarly, when using sequence information for detecting a single mismatch, a segment can be a twenty-five mer. The probability that the twenty-five mer would appear in a human genome with a single mismatch is calculated by multiplying the probability for a full match ($1 \div 4^{25}$) times the increased probability for mismatch at each nucleotide position (3 x 25). The probability that an eighteen mer with a single mismatch can be detected in an array for expression studies is approximately one in five. The probability that a twenty-mer with a single mismatch can be detected in a human genome is approximately one in five.

The term "open reading frame," ORF, means a series of nucleotide triplets coding for amino acids without any termination codons and is a sequence translatable into protein.

The terms "operably linked" or "operably associated" refer to functionally related nucleic acid sequences. For example, a promoter is operably associated or operably linked with a coding sequence if the promoter controls the transcription of the coding sequence. While operably linked nucleic acid sequences can be contiguous and in the same reading frame, certain genetic elements *e.g.* repressor genes are not contiguously linked to the coding sequence but still control transcription/translation of the coding sequence.

The term "pluripotent" refers to the capability of a cell to differentiate into a number of differentiated cell types that are present in an adult organism. A pluripotent cell is restricted in its differentiation capability in comparison to a totipotent cell.

The terms "polypeptide" or "peptide" or "amino acid sequence" refer to an oligopeptide, peptide, polypeptide or protein sequence or fragment thereof and to naturally occurring or synthetic molecules. A polypeptide "fragment," "portion," or "segment" is a stretch of amino acid residues of at least about 5 amino acids, preferably at least about 7 amino acids, more preferably at least about 9 amino acids and most preferably at least about 17 or more amino acids. The peptide preferably is not greater than about 200 amino acids, more preferably less than 150 amino acids and most preferably less than 100 amino acids. Preferably the peptide is from about 5 to about 200 amino acids. To be active, any polypeptide must have sufficient length to display biological and/or immunological activity.

The term "naturally occurring polypeptide" refers to polypeptides produced by cells that have not been genetically engineered and specifically contemplates various polypeptides arising from post-translational modifications of the polypeptide including, but not limited to, acetylation, carboxylation, glycosylation, phosphorylation, lipidation and acylation.

The term "translated protein coding portion" means a sequence which encodes for the full length protein which may include any leader sequence or any processing sequence.

The term "mature protein coding sequence" means a sequence which encodes a peptide or protein without a signal or leader sequence. The "mature protein portion" means that portion of the protein which does not include a signal or leader sequence. The peptide may have been produced by processing in the cell which removes any leader/signal sequence. The mature protein portion may or may not include an initial methionine residue. The methionine residue may be removed from the protein during processing in the cell. The peptide may be produced synthetically or the protein may have been produced using a polynucleotide only encoding for the mature protein coding sequence.

The term "derivative" refers to polypeptides chemically modified by such techniques as ubiquitination, labeling (*e.g.*, with radionuclides or various enzymes), covalent polymer attachment such as pegylation (derivatization with polyethylene glycol) and insertion or substitution by chemical synthesis of amino acids such as ornithine, which do not normally occur in human proteins.

The term "variant"(or "analog") refers to any polypeptide differing from naturally occurring polypeptides by amino acid insertions, deletions, and substitutions, created using, *e g.*, recombinant DNA techniques. Guidance in determining which amino acid residues may be replaced, added or deleted without abolishing activities of interest, may be found by comparing the sequence of the particular polypeptide with that of homologous peptides and minimizing the number of amino acid sequence changes made in regions of high homology (conserved regions) or by replacing amino acids with consensus sequence.

Alternatively, recombinant variants encoding these same or similar polypeptides may be synthesized or selected by making use of the "redundancy" in the genetic code. Various codon substitutions, such as the silent changes which produce various restriction sites, may be introduced to optimize cloning into a plasmid or viral vector or expression in a particular prokaryotic or eukaryotic system. Mutations in the polynucleotide sequence may be reflected in the polypeptide or domains of other peptides added to the polypeptide to modify the properties of any part of the polypeptide, to change characteristics such as ligand-binding affinities, interchain affinities, or degradation/turnover rate.

Preferably, amino acid "substitutions" are the result of replacing one amino acid with another amino acid having similar structural and/or chemical properties, *i.e.*, conservative amino acid replacements. "Conservative" amino acid substitutions may be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity, and/or the amphipathic nature of the residues involved. For example, nonpolar (hydrophobic) amino acids include alanine, leucine, isoleucine, valine, proline, phenylalanine, tryptophan, and methionine; polar neutral amino acids include glycine, serine, threonine, cysteine, tyrosine, asparagine, and glutamine; positively charged (basic) amino acids include arginine, lysine, and histidine; and negatively charged (acidic) amino acids include aspartic acid and glutamic acid. "Insertions" or "deletions" are preferably in the range of about 1 to 20 amino acids, more preferably 1 to 10 amino acids. The variation allowed may be experimentally determined by systematically making insertions, deletions, or substitutions of amino acids in a polypeptide molecule using recombinant DNA techniques and assaying the resulting recombinant variants for activity.

Alternatively, where alteration of function is desired, insertions, deletions or non-conservative alterations can be engineered to produce altered polypeptides. Such alterations

can, for example, alter one or more of the biological functions or biochemical characteristics of the polypeptides of the invention. For example, such alterations may change polypeptide characteristics such as ligand-binding affinities, interchain affinities, or degradation/turnover rate. Further, such alterations can be selected so as to generate polypeptides that are better suited for expression, scale up and the like in the host cells chosen for expression. For example, cysteine residues can be deleted or substituted with another amino acid residue in order to eliminate disulfide bridges.

The terms "purified" or "substantially purified" as used herein denotes that the indicated nucleic acid or polypeptide is present in the substantial absence of other biological macromolecules, *e.g.*, polynucleotides, proteins, and the like. In one embodiment, the polynucleotide or polypeptide is purified such that it constitutes at least 95% by weight, more preferably at least 99% by weight, of the indicated biological macromolecules present (but water, buffers, and other small molecules, especially molecules having a molecular weight of less than 1000 daltons, can be present).

The term "isolated" as used herein refers to a nucleic acid or polypeptide separated from at least one other component (*e.g.*, nucleic acid or polypeptide) present with the nucleic acid or polypeptide in its natural source. In one embodiment, the nucleic acid or polypeptide is found in the presence of (if anything) only a solvent, buffer, ion, or other component normally present in a solution of the same. The terms "isolated" and "purified" do not encompass nucleic acids or polypeptides present in their natural source.

The term "recombinant," when used herein to refer to a polypeptide or protein, means that a polypeptide or protein is derived from recombinant (*e.g.*, microbial, insect, or mammalian) expression systems. "Microbial" refers to recombinant polypeptides or proteins made in bacterial or fungal (*e.g.*, yeast) expression systems. As a product, "recombinant microbial" defines a polypeptide or protein essentially free of native endogenous substances and unaccompanied by associated native glycosylation. Polypeptides or proteins expressed in most bacterial cultures, *e.g.*, *E. coli*, will be free of glycosylation modifications; polypeptides or proteins expressed in yeast will have a glycosylation pattern in general different from those expressed in mammalian cells.

The term "recombinant expression vehicle or vector" refers to a plasmid or phage or virus or vector, for expressing a polypeptide from a DNA (RNA) sequence. An expression vehicle can comprise a transcriptional unit comprising an assembly of (1) a genetic element or elements having a regulatory role in gene expression, for example, promoters or enhancers, (2) a structural or coding sequence which is transcribed into mRNA and translated into protein, and (3) appropriate transcription initiation and termination sequences. Structural units intended for use

in yeast or eukaryotic expression systems preferably include a leader sequence enabling extracellular secretion of translated protein by a host cell. Alternatively, where recombinant protein is expressed without a leader or transport sequence, it may include an amino terminal methionine residue. This residue may or may not be subsequently cleaved from the expressed recombinant protein to provide a final product.

The term "recombinant expression system" means host cells which have stably integrated a recombinant transcriptional unit into chromosomal DNA or carry the recombinant transcriptional unit extrachromosomally. Recombinant expression systems as defined herein will express heterologous polypeptides or proteins upon induction of the regulatory elements linked to the DNA segment or synthetic gene to be expressed. This term also means host cells which have stably integrated a recombinant genetic element or elements having a regulatory role in gene expression, for example, promoters or enhancers. Recombinant expression systems as defined herein will express polypeptides or proteins endogenous to the cell upon induction of the regulatory elements linked to the endogenous DNA segment or gene to be expressed. The cells can be prokaryotic or eukaryotic.

The term "secreted" includes a protein that is transported across or through a membrane, including transport as a result of signal sequences in its amino acid sequence when it is expressed in a suitable host cell. "Secreted" proteins include without limitation proteins secreted wholly (*e.g.*, soluble proteins) or partially (*e.g.*, receptors) from the cell in which they are expressed. "Secreted" proteins also include without limitation proteins that are transported across the membrane of the endoplasmic reticulum. "Secreted" proteins are also intended to include proteins containing non-typical signal sequences (*e.g.* Interleukin-1 Beta, see Krasney, P.A. and Young, P.R. (1992) Cytokine 4(2):134 -143) and factors released from damaged cells (*e.g.* Interleukin-1 Receptor Antagonist, see Arend, W.P. et. al. (1998) Annu. Rev. Immunol. 16:27-55)

Where desired, an expression vector may be designed to contain a "signal or leader sequence" which will direct the polypeptide through the membrane of a cell. Such a sequence may be naturally present on the polypeptides of the present invention or provided from heterologous protein sources by recombinant DNA techniques.

The term "stringent" is used to refer to conditions that are commonly understood in the art as stringent. Stringent conditions can include highly stringent conditions (*i.e.*, hybridization to filter-bound DNA in 0.5 M $NaHPO_4$, 7% sodium dodecyl sulfate (SDS), 1 mM EDTA at 65°C, and washing in 0.1X SSC/0.1% SDS at 68°C), and moderately stringent conditions (*i.e.*, washing in 0.2X SSC/0.1% SDS at 42°C). Other exemplary hybridization conditions are described herein in the examples.

In instances of hybridization of deoxyoligonucleotides, additional exemplary stringent hybridization conditions include washing in 6X SSC/0.05% sodium pyrophosphate at 37°C (for 14-base oligonucleotides), 48°C (for 17-base oligos), 55°C (for 20-base oligonucleotides), and 60°C (for 23-base oligonucleotides).

As used herein, "substantially equivalent" can refer both to nucleotide and amino acid sequences, for example a mutant sequence, that varies from a reference sequence by one or more substitutions, deletions, or additions, the net effect of which does not result in an adverse functional dissimilarity between the reference and subject sequences. Typically, such a substantially equivalent sequence varies from one of those listed herein by no more than about 35% (*i.e.*, the number of individual residue substitutions, additions, and/or deletions in a substantially equivalent sequence, as compared to the corresponding reference sequence, divided by the total number of residues in the substantially equivalent sequence is about 0.35 or less). Such a sequence is said to have 65% sequence identity to the listed sequence. In one embodiment, a substantially equivalent, *e.g.*, mutant, sequence of the invention varies from a listed sequence by no more than 30% (70% sequence identity); in a variation of this embodiment, by no more than 25% (75% sequence identity); and in a further variation of this embodiment, by no more than 20% (80% sequence identity) and in a further variation of this embodiment, by no more than 10% (90% sequence identity) and in a further variation of this embodiment, by no more that 5% (95% sequence identity). Substantially equivalent, *e.g.*, mutant, amino acid sequences according to the invention preferably have at least 80% sequence identity with a listed amino acid sequence, more preferably at least 85% sequence identity, more preferably at least 90% sequence identity, more preferably at least 95% identity, more preferably at least 98% identity, and most preferably at least 99% identity. Substantially equivalent nucleotide sequences of the invention can have lower percent sequence identities, taking into account, for example, the redundancy or degeneracy of the genetic code. Preferably, nucleotide sequence has at least about 65% identity, more preferably at least about 75% identity, more preferably at least about 80% sequence identity, more preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, and most preferably at least about 95% identity, more preferably at least about 98% sequence identity, and most preferably at least about 99% sequence identity. For the purposes of the present invention, sequences having substantially equivalent biological activity and substantially equivalent expression characteristics are considered substantially equivalent. For the purposes of determining equivalence, truncation of the mature sequence (*e.g.*, via a mutation which creates a spurious stop codon) should be disregarded. Sequence identity may be determined, *e.g.*, using the Jotun Hein method (Hein, J.

(1990) Methods Enzymol. 183:626-645). Identity between sequences can also be determined by other methods known in the art, *e.g.* by varying hybridization conditions.

The term "totipotent" refers to the capability of a cell to differentiate into all of the cell types of an adult organism.

The term "transformation" means introducing DNA into a suitable host cell so that the DNA is replicable, either as an extrachromosomal element, or by chromosomal integration. The term "transfection" refers to the taking up of an expression vector by a suitable host cell, whether or not any coding sequences are in fact expressed. The term "infection" refers to the introduction of nucleic acids into a suitable host cell by use of a virus or viral vector.

As used herein, an "uptake modulating fragment," UMF, means a series of nucleotides which mediate the uptake of a linked DNA fragment into a cell. UMFs can be readily identified using known UMFs as a target sequence or target motif with the computer-based systems described below. The presence and activity of a UMF can be confirmed by attaching the suspected UMF to a marker sequence. The resulting nucleic acid molecule is then incubated with an appropriate host under appropriate conditions and the uptake of the marker sequence is determined. As described above, a UMF will increase the frequency of uptake of a linked marker sequence.

Each of the above terms is meant to encompass all that is described for each, unless the context dictates otherwise.

4.2 NUCLEIC ACIDS OF THE INVENTION

Nucleotide sequences of the invention are set forth in the Sequence Listing.

The isolated polynucleotides of the invention include a polynucleotide comprising the nucleotide sequences of SEQ ID NO: 1-30368; a polynucleotide encoding any one of the peptide sequences of SEQ ID NO: 30369-60736; and a polynucleotide comprising the nucleotide sequence encoding the mature protein coding sequence of the polypeptides of any one of SEQ ID NO: 30369-60736. The polynucleotides of the present invention also include, but are not limited to, a polynucleotide that hybridizes under stringent conditions to (a) the complement of any of the nucleotides sequences of SEQ ID NO: 1-30368; (b) nucleotide sequences encoding any one of the amino acid sequences set forth in the Sequence Listing; (c) a polynucleotide which is an allelic variant of any polynucleotide recited above; (d) a polynucleotide which encodes a species homolog of any of the proteins recited above; or (e) a polynucleotide that encodes a polypeptide comprising a specific domain or truncation of the polypeptides of SEQ ID NO: 30369-60736. Domains of interest may depend on the nature of the encoded polypeptide; *e.g.*, domains in receptor-like polypeptides include ligand-binding, extracellular, transmembrane, or cytoplasmic

domains, or combinations thereof; domains in immunoglobulin-like proteins include the variable immunoglobulin-like domains; domains in enzyme-like polypeptides include catalytic and substrate binding domains; and domains in ligand polypeptides include receptor-binding domains.

The polynucleotides of the invention include naturally occurring or wholly or partially synthetic DNA, *e.g.*, cDNA and genomic DNA, and RNA, *e.g.*, mRNA. The polynucleotides may include all of the coding region of the cDNA or may represent a portion of the coding region of the cDNA.

The present invention also provides genes corresponding to the cDNA sequences disclosed herein. The corresponding genes can be isolated in accordance with known methods using the sequence information disclosed herein. Such methods include the preparation of probes or primers from the disclosed sequence information for identification and/or amplification of genes in appropriate genomic libraries or other sources of genomic materials. Further 5' and 3' sequence can be obtained using methods known in the art. For example, full length cDNA or genomic DNA that corresponds to any of the polynucleotides of SEQ ID NO: 1-30368 can be obtained by screening appropriate cDNA or genomic DNA libraries under suitable hybridization conditions using any of the polynucleotides of SEQ ID NO: 1-30368 or a portion thereof as a probe. Alternatively, the polynucleotides of SEQ ID NO: 1-30368 may be used as the basis for suitable primer(s) that allow identification and/or amplification of genes in appropriate genomic DNA or cDNA libraries.

The nucleic acid sequences of the invention can be assembled from ESTs and sequences (including cDNA and genomic sequences) obtained from one or more public databases, such as dbEST, gbpri, and UniGene. The EST sequences can provide identifying sequence information, representative fragment or segment information, or novel segment information for the full-length gene.

The polynucleotides of the invention also provide polynucleotides including nucleotide sequences that are substantially equivalent to the polynucleotides recited above. Polynucleotides according to the invention can have, *e.g.*, at least about 65%, at least about 70%, at least about 75%, at least about 80%, 81%, 82%, 83%, 84%, more typically at least about 85%, 86%, 87%, 88%, 89%, more typically at least about 90%, 91%, 92%, 93%, 94%, and even more typically at least about 95%, 96%, 97%, 98%, 99%, sequence identity to a polynucleotide recited above.

Included within the scope of the nucleic acid sequences of the invention are nucleic acid sequence fragments that hybridize under stringent conditions to any of the nucleotide sequences of SEQ ID NO: 1-30368, or complements thereof, which fragment is greater than about 5 nucleotides, preferably 7 nucleotides, more preferably greater than 9 nucleotides and most preferably greater than 17 nucleotides. Fragments of, *e.g.* 15, 17, or 20 nucleotides or more that

are selective for (*i.e.* specifically hybridize to any one of the polynucleotides of the invention) are contemplated. Probes capable of specifically hybridizing to a polynucleotide can differentiate polynucleotide sequences of the invention from other polynucleotide sequences in the same family of genes or can differentiate human genes from genes of other species, and are preferably based on unique nucleotide sequences.

The sequences falling within the scope of the present invention are not limited to these specific sequences, but also include allelic and species variations thereof. Allelic and species variations can be routinely determined by comparing the sequence provided in SEQ ID NO: 1-30368, a representative fragment thereof, or a nucleotide sequence at least 90% identical, preferably 95% identical, to SEQ ID NO: 1-30368 with a sequence from another isolate of the same species. Furthermore, to accommodate codon variability, the invention includes nucleic acid molecules coding for the same amino acid sequences as do the specific ORFs disclosed herein. In other words, in the coding region of an ORF, substitution of one codon for another codon that encodes the same amino acid is expressly contemplated.

The nearest neighbor or homology result for the nucleic acids of the present invention, including SEQ ID NO: 1-30368 can be obtained by searching a database using an algorithm or a program. Preferably, a BLAST which stands for Basic Local Alignment Search Tool is used to search for local sequence alignments (Altshul, S.F. J Mol. Evol. 36 290-300 (1993) and Altschul S.F. et al. J. Mol. Biol. 21:403-410 (1990)). Alternatively a FASTA version 3 search against Genpept, using Fastxy algorithm.

Species homologs (or orthologs) of the disclosed polynucleotides and proteins are also provided by the present invention. Species homologs may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source from the desired species.

The invention also encompasses allelic variants of the disclosed polynucleotides or proteins; that is, naturally occurring alternative forms of the isolated polynucleotide which also encode proteins which are identical, homologous or related to that encoded by the polynucleotides.

The nucleic acid sequences of the invention are further directed to sequences which encode variants of the described nucleic acids. These amino acid sequence variants may be prepared by methods known in the art by introducing appropriate nucleotide changes into a native or variant polynucleotide. There are two variables in the construction of amino acid sequence variants: the location of the mutation and the nature of the mutation. Nucleic acids encoding the amino acid sequence variants are preferably constructed by mutating the polynucleotide to encode an amino acid sequence that does not occur in nature. These nucleic

acid alterations can be made at sites that differ in the nucleic acids from different species (variable positions) or in highly conserved regions (constant regions). Sites at such locations will typically be modified in series, *e.g.*, by substituting first with conservative choices (*e.g.*, hydrophobic amino acid to a different hydrophobic amino acid) and then with more distant choices (*e.g.*, hydrophobic amino acid to a charged amino acid), and then deletions or insertions may be made at the target site. Amino acid sequence deletions generally range from about 1 to 30 residues, preferably about 1 to 10 residues, and are typically contiguous. Amino acid insertions include amino- and/or carboxyl-terminal fusions ranging in length from one to one hundred or more residues, as well as intrasequence insertions of single or multiple amino acid residues. Intrasequence insertions may range generally from about 1 to 10 amino residues, preferably from 1 to 5 residues. Examples of terminal insertions include the heterologous signal sequences necessary for secretion or for intracellular targeting in different host cells and sequences such as FLAG or poly-histidine sequences useful for purifying the expressed protein.

In a preferred method, polynucleotides encoding the novel amino acid sequences are changed via site-directed mutagenesis. This method uses oligonucleotide sequences to alter a polynucleotide to encode the desired amino acid variant, as well as sufficient adjacent nucleotides on both sides of the changed amino acid to form a stable duplex on either side of the site of being changed. In general, the techniques of site-directed mutagenesis are well known to those of skill in the art and this technique is exemplified by publications such as, Edelman et al., *DNA* 2:183 (1983). A versatile and efficient method for producing site-specific changes in a polynucleotide sequence was published by Zoller and Smith, *Nucleic Acids Res.* 10:6487-6500 (1982). PCR may also be used to create amino acid sequence variants of the novel nucleic acids. When small amounts of template DNA are used as starting material, primer(s) that differs slightly in sequence from the corresponding region in the template DNA can generate the desired amino acid variant. PCR amplification results in a population of product DNA fragments that differ from the polynucleotide template encoding the polypeptide at the position specified by the primer. The product DNA fragments replace the corresponding region in the plasmid and this gives a polynucleotide encoding the desired amino acid variant.

A further technique for generating amino acid variants is the cassette mutagenesis technique described in Wells et al., *Gene* 34:315 (1985); and other mutagenesis techniques well known in the art, such as, for example, the techniques in Sambrook et al., supra, and *Current Protocols in Molecular Biology*, Ausubel et al. Due to the inherent degeneracy of the genetic code, other DNA sequences which encode substantially the same or a functionally equivalent amino acid sequence may be used in the practice of the invention for the cloning and expression

of these novel nucleic acids. Such DNA sequences include those which are capable of hybridizing to the appropriate novel nucleic acid sequence under stringent conditions.

Polynucleotides encoding preferred polypeptide truncations of the invention can be used to generate polynucleotides encoding chimeric or fusion proteins comprising one or more domains of the invention and heterologous protein sequences.

The polynucleotides of the invention additionally include the complement of any of the polynucleotides recited above. The polynucleotide can be DNA (genomic, cDNA, amplified, or synthetic) or RNA. Methods and algorithms for obtaining such polynucleotides are well known to those of skill in the art and can include, for example, methods for determining hybridization conditions that can routinely isolate polynucleotides of the desired sequence identities.

In accordance with the invention, polynucleotide sequences comprising the mature protein coding sequences corresponding to any one of SEQ ID NO: 1-30368, or functional equivalents thereof, may be used to generate recombinant DNA molecules that direct the expression of that nucleic acid, or a functional equivalent thereof, in appropriate host cells. Also included are the cDNA inserts of any of the clones identified herein.

A polynucleotide according to the invention can be joined to any of a variety of other nucleotide sequences by well-established recombinant DNA techniques (see Sambrook J et al. (1989) Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, NY). Useful nucleotide sequences for joining to polynucleotides include an assortment of vectors, *e.g.*, plasmids, cosmids, lambda phage derivatives, phagemids, and the like, that are well known in the art. Accordingly, the invention also provides a vector including a polynucleotide of the invention and a host cell containing the polynucleotide. In general, the vector contains an origin of replication functional in at least one organism, convenient restriction endonuclease sites, and a selectable marker for the host cell. Vectors according to the invention include expression vectors, replication vectors, probe generation vectors, and sequencing vectors. A host cell according to the invention can be a prokaryotic or eukaryotic cell and can be a unicellular organism or part of a multicellular organism.

The present invention further provides recombinant constructs comprising a nucleic acid having any of the nucleotide sequences of SEQ ID NO: 1-30368 or a fragment thereof or any other polynucleotides of the invention. In one embodiment, the recombinant constructs of the present invention comprise a vector, such as a plasmid or viral vector, into which a nucleic acid having any of the nucleotide sequences of SEQ ID NO: 1-30368 or a fragment thereof is inserted, in a forward or reverse orientation. In the case of a vector comprising one of the ORFs of the present invention, the vector may further comprise regulatory sequences, including for example, a promoter, operably linked to the ORF. Large numbers of suitable vectors and

promoters are known to those of skill in the art and are commercially available for generating the recombinant constructs of the present invention. The following vectors are provided by way of example. Bacterial: pBs, phagescript, PsiX174, pBluescript SK, pBs KS, pNH8a, pNH16a, pNH18a, pNH46a (Stratagene); pTrc99A, pKK223-3, pKK233-3, pDR540, pRIT5 (Pharmacia). Eukaryotic: pWLneo, pSV2cat, pOG44, PXTI, pSG (Stratagene) pSVK3, pBPV, pMSG, pSVL (Pharmacia).

The isolated polynucleotide of the invention may be operably linked to an expression control sequence such as the pMT2 or pED expression vectors disclosed in Kaufman et al., *Nucleic Acids Res.* 19, 4485-4490 (1991), in order to produce the protein recombinantly. Many suitable expression control sequences are known in the art. General methods of expressing recombinant proteins are also known and are exemplified in R. Kaufman, *Methods in Enzymology* 185, 537-566 (1990). As defined herein "operably linked" means that the isolated polynucleotide of the invention and an expression control sequence are situated within a vector or cell in such a way that the protein is expressed by a host cell which has been transformed (transfected) with the ligated polynucleotide/expression control sequence.

Promoter regions can be selected from any desired gene using CAT (chloramphenicol transferase) vectors or other vectors with selectable markers. Two appropriate vectors are pKK232-8 and pCM7. Particular named bacterial promoters include lacI, lacZ, T3, T7, gpt, lambda PR, and trc. Eukaryotic promoters include CMV immediate early, HSV thymidine kinase, early and late SV40, LTRs from retrovirus, and mouse metallothionein-I. Selection of the appropriate vector and promoter is well within the level of ordinary skill in the art. Generally, recombinant expression vectors will include origins of replication and selectable markers permitting transformation of the host cell, *e.g.*, the ampicillin resistance gene of *E. coli* and *S. cerevisiae* TRP1 gene, and a promoter derived from a highly-expressed gene to direct transcription of a downstream structural sequence. Such promoters can be derived from operons encoding glycolytic enzymes such as 3-phosphoglycerate kinase (PGK), a-factor, acid phosphatase, or heat shock proteins, among others. The heterologous structural sequence is assembled in appropriate phase with translation initiation and termination sequences, and preferably, a leader sequence capable of directing secretion of translated protein into the periplasmic space or extracellular medium. Optionally, the heterologous sequence can encode a fusion protein including an amino terminal identification peptide imparting desired characteristics, *e.g.*, stabilization or simplified purification of expressed recombinant product. Useful expression vectors for bacterial use are constructed by inserting a structural DNA sequence encoding a desired protein together with suitable translation initiation and termination signals in operable reading phase with a functional promoter. The vector will comprise one or

more phenotypic selectable markers and an origin of replication to ensure maintenance of the vector and to, if desirable, provide amplification within the host. Suitable prokaryotic hosts for transformation include *E. coli*, *Bacillus subtilis*, *Salmonella typhimurium* and various species within the genera *Pseudomonas*, *Streptomyces*, and *Staphylococcus*, although others may also be employed as a matter of choice.

As a representative but non-limiting example, useful expression vectors for bacterial use can comprise a selectable marker and bacterial origin of replication derived from commercially available plasmids comprising genetic elements of the well known cloning vector pBR322 (ATCC 37017). Such commercial vectors include, for example, pKK223-3 (Pharmacia Fine Chemicals, Uppsala, Sweden) and GEM 1 (Promega Biotech, Madison, WI, USA). These pBR322 "backbone" sections are combined with an appropriate promoter and the structural sequence to be expressed. Following transformation of a suitable host strain and growth of the host strain to an appropriate cell density, the selected promoter is induced or derepressed by appropriate means (*e.g.*, temperature shift or chemical induction) and cells are cultured for an additional period. Cells are typically harvested by centrifugation, disrupted by physical or chemical means, and the resulting crude extract retained for further purification.

Polynucleotides of the invention can also be used to induce immune responses. For example, as described in Fan et al., *Nat. Biotech.* 17:870-872 (1999), incorporated herein by reference, nucleic acid sequences encoding a polypeptide may be used to generate antibodies against the encoded polypeptide following topical administration of naked plasmid DNA or following injection, and preferably intramuscular injection of the DNA. The nucleic acid sequences are preferably inserted in a recombinant expression vector and may be in the form of naked DNA.

4.3 ANTISENSE

Another aspect of the invention pertains to isolated antisense nucleic acid molecules that are hybridizable to or complementary to the nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 1-30368, or fragments, analogs or derivatives thereof. An "antisense" nucleic acid comprises a nucleotide sequence that is complementary to a "sense" nucleic acid encoding a protein, *e.g.*, complementary to the coding strand of a double-stranded cDNA molecule or complementary to an mRNA sequence. In specific aspects, antisense nucleic acid molecules are provided that comprise a sequence complementary to at least about 10, 25, 50, 100, 250 or 500 nucleotides or an entire coding strand, or to only a portion thereof. Nucleic acid molecules encoding fragments, homologs, derivatives and analogs of a protein of any of SEQ ID

NO: 30369-60736 or antisense nucleic acids complementary to a nucleic acid sequence of SEQ ID NO: 1-30368 are additionally provided.

In one embodiment, an antisense nucleic acid molecule is antisense to a "coding region" of the coding strand of a nucleotide sequence of the invention. The term "coding region" refers to the region of the nucleotide sequence comprising codons which are translated into amino acid residues. In another embodiment, the antisense nucleic acid molecule is antisense to a "noncoding region" of the coding strand of a nucleotide sequence of the invention. The term "noncoding region" refers to 5' and 3' sequences which flank the coding region that are not translated into amino acids (*i.e.*, also referred to as 5' and 3' untranslated regions).

Given the coding strand sequences encoding a nucleic acid disclosed herein (*e.g.*, SEQ ID NO: 1-30368), antisense nucleic acids of the invention can be designed according to the rules of Watson and Crick or Hoogsteen base pairing. The antisense nucleic acid molecule can be complementary to the entire coding region of a mRNA, but more preferably is an oligonucleotide that is antisense to only a portion of the coding or noncoding region of a mRNA. For example, the antisense oligonucleotide can be complementary to the region surrounding the translation start site of a mRNA. An antisense oligonucleotide can be, for example, about 5, 10, 15, 20, 25, 30, 35, 40, 45 or 50 nucleotides in length. An antisense nucleic acid of the invention can be constructed using chemical synthesis or enzymatic ligation reactions using procedures known in the art. For example, an antisense nucleic acid (*e.g.*, an antisense oligonucleotide) can be chemically synthesized using naturally occurring nucleotides or variously modified nucleotides designed to increase the biological stability of the molecules or to increase the physical stability of the duplex formed between the antisense and sense nucleic acids, *e.g.*, phosphorothioate derivatives and acridine substituted nucleotides can be used.

Examples of modified nucleotides that can be used to generate the antisense nucleic acid include: 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xanthine, 4-acetylcytosine, 5-(carboxyhydroxylmethyl) uracil, 5-carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluracil, dihydrouracil, beta-D-galactosylqueosine, inosine, N6-isopentenyladenine, 1-methylguanine, 1-methylinosine, 2,2-dimethylguanine, 2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N6-adenine, 7-methylguanine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil, beta-D-mannosylqueosine, 5'-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methylthio-N6-isopentenyladenine, uracil-5-oxyacetic acid (v), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5-oxyacetic acid methylester, uracil-5-oxyacetic acid (v), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil, (acp3)w, and 2,6-diaminopurine. Alternatively, the

antisense nucleic acid can be produced biologically using an expression vector into which a nucleic acid has been subcloned in an antisense orientation (*i.e.*, RNA transcribed from the inserted nucleic acid will be of an antisense orientation to a target nucleic acid of interest, described further in the following subsection).

The antisense nucleic acid molecules of the invention are typically administered to a subject or generated *in situ* such that they hybridize with or bind to cellular mRNA and/or genomic DNA encoding a protein according to the invention to thereby inhibit expression of the protein, *e.g.*, by inhibiting transcription and/or translation. The hybridization can be by conventional nucleotide complementarity to form a stable duplex, or, for example, in the case of an antisense nucleic acid molecule that binds to DNA duplexes, through specific interactions in the major groove of the double helix. An example of a route of administration of antisense nucleic acid molecules of the invention includes direct injection at a tissue site. Alternatively, antisense nucleic acid molecules can be modified to target selected cells and then administered systemically. For example, for systemic administration, antisense molecules can be modified such that they specifically bind to receptors or antigens expressed on a selected cell surface, *e.g.*, by linking the antisense nucleic acid molecules to peptides or antibodies that bind to cell surface receptors or antigens. The antisense nucleic acid molecules can also be delivered to cells using the vectors described herein. To achieve sufficient intracellular concentrations of antisense molecules, vector constructs in which the antisense nucleic acid molecule is placed under the control of a strong pol II or pol III promoter are preferred.

In yet another embodiment, the antisense nucleic acid molecule of the invention is an -anomeric nucleic acid molecule. An -anomeric nucleic acid molecule forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual -units, the strands run parallel to each other (Gaultier *et al.* (1987) *Nucleic Acids Res* 15: 6625-6641). The antisense nucleic acid molecule can also comprise a 2'-o-methylribonucleotide (Inoue *et al.* (1987) *Nucleic Acids Res* 15: 6131-6148) or a chimeric RNA -DNA analogue (Inoue *et al.* (1987) *FEBS Lett* 215: 327-330).

4.4 RIBOZYMES AND PNA MOIETIES

In still another embodiment, an antisense nucleic acid of the invention is a ribozyme. Ribozymes are catalytic RNA molecules with ribonuclease activity that are capable of cleaving a single-stranded nucleic acid, such as a mRNA, to which they have a complementary region. Thus, ribozymes (*e.g.*, hammerhead ribozymes (described in Haselhoff and Gerlach (1988) *Nature* 334:585-591)) can be used to catalytically cleave a mRNA transcripts to thereby inhibit translation of a mRNA. A ribozyme having specificity for a nucleic acid of the invention can be

designed based upon the nucleotide sequence of a DNA disclosed herein (*i.e.*, SEQ ID NO: 1-30368). For example, a derivative of a Tetrahymena L-19 IVS RNA can be constructed in which the nucleotide sequence of the active site is complementary to the nucleotide sequence to be cleaved in an mRNA of SEQ ID NO: 1-30368 (see, *e.g.*, Cech *et al.* U.S. Pat. No. 4,987,071; and Cech *et al.* U.S. Pat. No. 5,116,742). Alternatively, polynucleotides of the invention can be used to select a catalytic RNA having a specific ribonuclease activity from a pool of RNA molecules. See, *e.g.*, Bartel *et al.*, (1993) *Science* 261:1411-1418.

Alternatively, gene expression can be inhibited by targeting nucleotide sequences complementary to the regulatory region (*e.g.*, promoter and/or enhancers) to form triple helical structures that prevent transcription of the gene in target cells. See generally, Helene. (1991) *Anticancer Drug Des.* 6: 569-84; Helene. *et al.* (1992) *Ann. N.Y. Acad. Sci.* 660:27-36; and Maher (1992) *Bioassays* 14: 807-15.

In various embodiments, the nucleic acids of the invention can be modified at the base moiety, sugar moiety or phosphate backbone to improve, *e.g.*, the stability, hybridization, or solubility of the molecule. For example, the deoxyribose phosphate backbone of the nucleic acids can be modified to generate peptide nucleic acids (see Hyrup *et al.* (1996) *Bioorg Med Chem* 4: 5-23). As used herein, the terms "peptide nucleic acids" or "PNAs" refer to nucleic acid mimics, *e.g.*, DNA mimics, in which the deoxyribose phosphate backbone is replaced by a pseudopeptide backbone and only the four natural nucleobases are retained. The neutral backbone of PNAs has been shown to allow for specific hybridization to DNA and RNA under conditions of low ionic strength. The synthesis of PNA oligomers can be performed using standard solid phase peptide synthesis protocols as described in Hyrup *et al.* (1996) above; Perry-O'Keefe *et al.* (1996) *PNAS* 93: 14670-675.

PNAs of the invention can be used in therapeutic and diagnostic applications. For example, PNAs can be used as antisense or antigene agents for sequence-specific modulation of gene expression by, *e.g.*, inducing transcription or translation arrest or inhibiting replication. PNAs of the invention can also be used, *e.g.*, in the analysis of single base pair mutations in a gene by, *e.g.*, PNA directed PCR clamping; as artificial restriction enzymes when used in combination with other enzymes, *e.g.*, S1 nucleases (Hyrup B. (1996) above); or as probes or primers for DNA sequence and hybridization (Hyrup *et al.* (1996), above; Perry-O'Keefe (1996), above).

In another embodiment, PNAs of the invention can be modified, *e.g.*, to enhance their stability or cellular uptake, by attaching lipophilic or other helper groups to PNA, by the formation of PNA-DNA chimeras, or by the use of liposomes or other techniques of drug delivery known in the art. For example, PNA-DNA chimeras can be generated that may

combine the advantageous properties of PNA and DNA. Such chimeras allow DNA recognition enzymes, *e.g.*, RNase H and DNA polymerases, to interact with the DNA portion while the PNA portion would provide high binding affinity and specificity. PNA-DNA chimeras can be linked using linkers of appropriate lengths selected in terms of base stacking, number of bonds between the nucleobases, and orientation (Hyrup (1996) above). The synthesis of PNA-DNA chimeras can be performed as described in Hyrup (1996) above and Finn *et al.* (1996) *Nucl Acids Res* 24: 3357-63. For example, a DNA chain can be synthesized on a solid support using standard phosphoramidite coupling chemistry, and modified nucleoside analogs, *e.g.*, 5'-(4-methoxytrityl)amino-5'-deoxy-thymidine phosphoramidite, can be used between the PNA and the 5' end of DNA (Mag *et al.* (1989) *Nucl Acid Res* 17: 5973-88). PNA monomers are then coupled in a stepwise manner to produce a chimeric molecule with a 5' PNA segment and a 3' DNA segment (Finn *et al.* (1996) above). Alternatively, chimeric molecules can be synthesized with a 5′ DNA segment and a 3′ PNA segment. See, Petersen *et al.* (1975) *Bioorg Med Chem Lett* 5: 1119-11124.

In other embodiments, the oligonucleotide may include other appended groups such as peptides (*e.g.*, for targeting host cell receptors *in vivo*), or agents facilitating transport across the cell membrane (see, *e.g.*, Letsinger *et al.*, 1989, *Proc. Natl. Acad. Sci. U.S.A.* 86:6553-6556; Lemaitre *et al.*, 1987, Proc. *Natl. Acad. Sci.* 84:648-652; PCT Publication No. W088/09810) or the blood-brain barrier (see, *e.g.*, PCT Publication No. W089/10134). In addition, oligonucleotides can be modified with hybridization triggered cleavage agents (See, *e.g.*, Krol *et al.*, 1988, *BioTechniques* 6:958-976) or intercalating agents (see, *e.g.*, Zon, 1988, *Pharm. Res.* 5:539-549). To this end, the oligonucleotide may be conjugated to another molecule, *e.g.*, a peptide, a hybridization triggered cross-linking agent, a transport agent, a hybridization-triggered cleavage agent, etc.

4.5 HOSTS

The present invention further provides host cells genetically engineered to contain the polynucleotides of the invention. For example, such host cells may contain nucleic acids of the invention introduced into the host cell using known transformation, transfection or infection methods. The present invention still further provides host cells genetically engineered to express the polynucleotides of the invention, wherein such polynucleotides are in operative association with a regulatory sequence heterologous to the host cell which drives expression of the polynucleotides in the cell.

Knowledge of nucleic acid sequences allows for modification of cells to permit, or increase, expression of endogenous polypeptide. Cells can be modified (*e.g.*, by homologous

recombination) to provide increased polypeptide expression by replacing, in whole or in part, the naturally occurring promoter with all or part of a heterologous promoter so that the cells express the polypeptide at higher levels. The heterologous promoter is inserted in such a manner that it is operatively linked to the encoding sequences. See, for example, PCT International Publication No. WO94/12650, PCT International Publication No. WO92/20808, and PCT International Publication No. WO91/09955. It is also contemplated that, in addition to heterologous promoter DNA, amplifiable marker DNA (*e.g.*, ada, dhfr, and the multifunctional CAD gene which encodes carbamyl phosphate synthase, aspartate transcarbamylase, and dihydroorotase) and/or intron DNA may be inserted along with the heterologous promoter DNA. If linked to the coding sequence, amplification of the marker DNA by standard selection methods results in co-amplification of the desired protein coding sequences in the cells.

The host cell can be a higher eukaryotic host cell, such as a mammalian cell, a lower eukaryotic host cell, such as a yeast cell, or the host cell can be a prokaryotic cell, such as a bacterial cell. Introduction of the recombinant construct into the host cell can be effected by calcium phosphate transfection, DEAE, dextran mediated transfection, or electroporation (Davis, L. et al., *Basic Methods in Molecular Biology* (1986)). The host cells containing one of the polynucleotides of the invention, can be used in conventional manners to produce the gene product encoded by the isolated fragment (in the case of an ORF) or can be used to produce a heterologous protein under the control of the EMF.

Any host/vector system can be used to express one or more of the ORFs of the present invention. These include, but are not limited to, eukaryotic hosts such as HeLa cells, Cv-1 cell, COS cells, 293 cells, and Sf9 cells, as well as prokaryotic host such as *E. coli* and *B. subtilis*. The most preferred cells are those which do not normally express the particular polypeptide or protein or which expresses the polypeptide or protein at low natural level. Mature proteins can be expressed in mammalian cells, yeast, bacteria, or other cells under the control of appropriate promoters. Cell-free translation systems can also be employed to produce such proteins using RNAs derived from the DNA constructs of the present invention. Appropriate cloning and expression vectors for use with prokaryotic and eukaryotic hosts are described by Sambrook, et al., in Molecular Cloning: A Laboratory Manual, Second Edition, Cold Spring Harbor, New York (1989), the disclosure of which is hereby incorporated by reference.

Various mammalian cell culture systems can also be employed to express recombinant protein. Examples of mammalian expression systems include the COS-7 lines of monkey kidney fibroblasts, described by Gluzman, Cell 23:175 (1981). Other cell lines capable of expressing a compatible vector are, for example, the C127, monkey COS cells, Chinese Hamster Ovary (CHO) cells, human kidney 293 cells, human epidermal A431 cells, human Colo205 cells, 3T3

cells, CV-1 cells, other transformed primate cell lines, normal diploid cells, cell strains derived from *in vitro* culture of primary tissue, primary explants, HeLa cells, mouse L cells, BHK, HL-60, U937, HaK or Jurkat cells. Mammalian expression vectors will comprise an origin of replication, a suitable promoter and also any necessary ribosome binding sites, polyadenylation site, splice donor and acceptor sites, transcriptional termination sequences, and 5′ flanking nontranscribed sequences. DNA sequences derived from the SV40 viral genome, for example, SV40 origin, early promoter, enhancer, splice, and polyadenylation sites may be used to provide the required nontranscribed genetic elements. Recombinant polypeptides and proteins produced in bacterial culture are usually isolated by initial extraction from cell pellets, followed by one or more salting-out, aqueous ion exchange or size exclusion chromatography steps. Protein refolding steps can be used, as necessary, in completing configuration of the mature protein. Finally, high performance liquid chromatography (HPLC) can be employed for final purification steps. Microbial cells employed in expression of proteins can be disrupted by any convenient method, including freeze-thaw cycling, sonication, mechanical disruption, or use of cell lysing agents.

Alternatively, it may be possible to produce the protein in lower eukaryotes such as yeast or insects or in prokaryotes such as bacteria. Potentially suitable yeast strains include *Saccharomyces cerevisiae*, *Schizosaccharomyces pombe*, *Kluyveromyces* strains, *Candida*, or any yeast strain capable of expressing heterologous proteins. Potentially suitable bacterial strains include *Escherichia coli, Bacillus subtilis, Salmonella typhimurium*, or any bacterial strain capable of expressing heterologous proteins. If the protein is made in yeast or bacteria, it may be necessary to modify the protein produced therein, for example by phosphorylation or glycosylation of the appropriate sites, in order to obtain the functional protein. Such covalent attachments may be accomplished using known chemical or enzymatic methods.

In another embodiment of the present invention, cells and tissues may be engineered to express an endogenous gene comprising the polynucleotides of the invention under the control of inducible regulatory elements, in which case the regulatory sequences of the endogenous gene may be replaced by homologous recombination. As described herein, gene targeting can be used to replace a gene's existing regulatory region with a regulatory sequence isolated from a different gene or a novel regulatory sequence synthesized by genetic engineering methods. Such regulatory sequences may be comprised of promoters, enhancers, scaffold-attachment regions, negative regulatory elements, transcriptional initiation sites, regulatory protein binding sites or combinations of said sequences. Alternatively, sequences which affect the structure or stability of the RNA or protein produced may be replaced, removed, added, or otherwise modified by targeting. These sequence include polyadenylation signals, mRNA stability elements, splice

sites, leader sequences for enhancing or modifying transport or secretion properties of the protein, or other sequences which alter or improve the function or stability of protein or RNA molecules.

The targeting event may be a simple insertion of the regulatory sequence, placing the gene under the control of the new regulatory sequence, *e.g.*, inserting a new promoter or enhancer or both upstream of a gene. Alternatively, the targeting event may be a simple deletion of a regulatory element, such as the deletion of a tissue-specific negative regulatory element. Alternatively, the targeting event may replace an existing element; for example, a tissue-specific enhancer can be replaced by an enhancer that has broader or different cell-type specificity than the naturally occurring elements. Here, the naturally occurring sequences are deleted and new sequences are added. In all cases, the identification of the targeting event may be facilitated by the use of one or more selectable marker genes that are contiguous with the targeting DNA, allowing for the selection of cells in which the exogenous DNA has integrated into the host cell genome. The identification of the targeting event may also be facilitated by the use of one or more marker genes exhibiting the property of negative selection, such that the negatively selectable marker is linked to the exogenous DNA, but configured such that the negatively selectable marker flanks the targeting sequence, and such that a correct homologous recombination event with sequences in the host cell genome does not result in the stable integration of the negatively selectable marker. Markers useful for this purpose include the Herpes Simplex Virus thymidine kinase (TK) gene or the bacterial xanthine-guanine phosphoribosyl-transferase (gpt) gene.

The gene targeting or gene activation techniques which can be used in accordance with this aspect of the invention are more particularly described in U.S. Patent No. 5,272,071 to Chappel; U.S. Patent No. 5,578,461 to Sherwin et al.; International Application No. PCT/US92/09627 (WO93/09222) by Selden et al.; and International Application No. PCT/US90/06436 (WO91/06667) by Skoultchi et al., each of which is incorporated by reference herein in its entirety.

4.6 POLYPEPTIDES OF THE INVENTION

The isolated polypeptides of the invention include, but are not limited to, a polypeptide comprising: the amino acid sequences set forth as any one of SEQ ID NO: 30369-60736 or an amino acid sequence encoded by any one of the nucleotide sequences SEQ ID NO: 1-30368 or the corresponding full length or mature protein. Polypeptides of the invention also include polypeptides preferably with biological or immunological activity that are encoded by: (a) a polynucleotide having any one of the nucleotide sequences set forth in SEQ ID NO: 1-30368 or

(b) polynucleotides encoding any one of the amino acid sequences set forth as SEQ ID NO: 30369-60736 or (c) polynucleotides that hybridize to the complement of the polynucleotides of either (a) or (b) under stringent hybridization conditions. The invention also provides biologically active or immunologically active variants of any of the amino acid sequences set forth as SEQ ID NO: 30369-60736 or the corresponding full length or mature protein; and "substantial equivalents" thereof (*e.g.*, with at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, 86%, 87%, 88%, 89%, at least about 90%, 91%, 92%, 93%, 94%, typically at least about 95%, 96%, 97%, more typically at least about 98%, or most typically at least about 99% amino acid identity) that retain biological activity. Polypeptides encoded by allelic variants may have a similar, increased, or decreased activity compared to polypeptides comprising SEQ ID NO: 30369-60736.

Fragments of the proteins of the present invention which are capable of exhibiting biological activity are also encompassed by the present invention. Fragments of the protein may be in linear form or they may be cyclized using known methods, for example, as described in H. U. Saragovi, et al., Bio/Technology 10, 773-778 (1992) and in R. S. McDowell, et al., J. Amer. Chem. Soc. 114, 9245-9253 (1992), both of which are incorporated herein by reference. Such fragments may be fused to carrier molecules such as immunoglobulins for many purposes, including increasing the valency of protein binding sites.

The present invention also provides both full-length and mature forms (for example, without a signal sequence or precursor sequence) of the disclosed proteins. The protein coding sequence is identified in the sequence listing by translation of the disclosed nucleotide sequences. The mature form of such protein may be obtained by expression of a full-length polynucleotide in a suitable mammalian cell or other host cell. The sequence of the mature form of the protein is also determinable from the amino acid sequence of the full-length form. Where proteins of the present invention are membrane bound, soluble forms of the proteins are also provided. In such forms, part or all of the regions causing the proteins to be membrane bound are deleted so that the proteins are fully secreted from the cell in which they are expressed.

Protein compositions of the present invention may further comprise an acceptable carrier, such as a hydrophilic, *e.g.*, pharmaceutically acceptable, carrier.

The present invention further provides isolated polypeptides encoded by the nucleic acid fragments of the present invention or by degenerate variants of the nucleic acid fragments of the present invention. By "degenerate variant" is intended nucleotide fragments which differ from a nucleic acid fragment of the present invention (*e.g.*, an ORF) by nucleotide sequence but, due to the degeneracy of the genetic code, encode an identical polypeptide sequence. Preferred nucleic acid fragments of the present invention are the ORFs that encode proteins.

A variety of methodologies known in the art can be utilized to obtain any one of the isolated polypeptides or proteins of the present invention. At the simplest level, the amino acid sequence can be synthesized using commercially available peptide synthesizers. The synthetically-constructed protein sequences, by virtue of sharing primary, secondary or tertiary structural and/or conformational characteristics with proteins may possess biological properties in common therewith, including protein activity. This technique is particularly useful in producing small peptides and fragments of larger polypeptides. Fragments are useful, for example, in generating antibodies against the native polypeptide. Thus, they may be employed as biologically active or immunological substitutes for natural, purified proteins in screening of therapeutic compounds and in immunological processes for the development of antibodies.

The polypeptides and proteins of the present invention can alternatively be purified from cells which have been altered to express the desired polypeptide or protein. As used herein, a cell is said to be altered to express a desired polypeptide or protein when the cell, through genetic manipulation, is made to produce a polypeptide or protein which it normally does not produce or which the cell normally produces at a lower level. One skilled in the art can readily adapt procedures for introducing and expressing either recombinant or synthetic sequences into eukaryotic or prokaryotic cells in order to generate a cell which produces one of the polypeptides or proteins of the present invention.

The invention also relates to methods for producing a polypeptide comprising growing a culture of host cells of the invention in a suitable culture medium, and purifying the protein from the cells or the culture in which the cells are grown. For example, the methods of the invention include a process for producing a polypeptide in which a host cell containing a suitable expression vector that includes a polynucleotide of the invention is cultured under conditions that allow expression of the encoded polypeptide. The polypeptide can be recovered from the culture, conveniently from the culture medium, or from a lysate prepared from the host cells and further purified. Preferred embodiments include those in which the protein produced by such process is a full length or mature form of the protein.

In an alternative method, the polypeptide or protein is purified from bacterial cells which naturally produce the polypeptide or protein. One skilled in the art can readily follow known methods for isolating polypeptides and proteins in order to obtain one of the isolated polypeptides or proteins of the present invention. These include, but are not limited to, immunochromatography, HPLC, size-exclusion chromatography, ion-exchange chromatography, and immuno-affinity chromatography. See, *e.g.*, Scopes, *Protein Purification: Principles and Practice*, Springer-Verlag (1994); Sambrook, et al., in Molecular Cloning: *A Laboratory Manual*; Ausubel et al., *Current Protocols in Molecular Biology*. Polypeptide fragments that

retain biological/immunological activity include fragments comprising greater than about 100 amino acids, or greater than about 200 amino acids, and fragments that encode specific protein domains.

The purified polypeptides can be used in *in vitro* binding assays which are well known in the art to identify molecules which bind to the polypeptides. These molecules include but are not limited to, for *e.g.*, small molecules, molecules from combinatorial libraries, antibodies or other proteins. The molecules identified in the binding assay are then tested for antagonist or agonist activity in *in vivo* tissue culture or animal models that are well known in the art. In brief, the molecules are titrated into a plurality of cell cultures or animals and then tested for either cell/animal death or prolonged survival of the animal/cells.

In addition, the peptides of the invention or molecules capable of binding to the peptides may be complexed with toxins, *e.g.*, ricin or cholera, or with other compounds that are toxic to cells. The toxin-binding molecule complex is then targeted to a tumor or other cell by the specificity of the binding molecule for SEQ ID NO: 30369-60736.

The protein of the invention may also be expressed as a product of transgenic animals, *e.g.*, as a component of the milk of transgenic cows, goats, pigs, or sheep which are characterized by somatic or germ cells containing a nucleotide sequence encoding the protein.

The proteins provided herein also include proteins characterized by amino acid sequences similar to those of purified proteins but into which modification are naturally provided or deliberately engineered. For example, modifications in the peptide or DNA sequence can be made by those skilled in the art using known techniques. Modifications of interest in the protein sequences may include the alteration, substitution, replacement, insertion or deletion of a selected amino acid residue in the coding sequence. For example, one or more of the cysteine residues may be deleted or replaced with another amino acid to alter the conformation of the molecule. Techniques for such alteration, substitution, replacement, insertion or deletion are well known to those skilled in the art (see, *e.g.*, U.S. Pat. No. 4,518,584). Preferably, such alteration, substitution, replacement, insertion or deletion retains the desired activity of the protein. Regions of the protein that are important for the protein function can be determined by various methods known in the art including the alanine-scanning method which involved systematic substitution of single or strings of amino acids with alanine, followed by testing the resulting alanine-containing variant for biological activity. This type of analysis determines the importance of the substituted amino acid(s) in biological activity. Regions of the protein that are important for protein function may be determined by the eMATRIX program.

Other fragments and derivatives of the sequences of proteins which would be expected to retain protein activity in whole or in part and are useful for screening or other immunological

methodologies may also be easily made by those skilled in the art given the disclosures herein. Such modifications are encompassed by the present invention.

The protein may also be produced by operably linking the isolated polynucleotide of the invention to suitable control sequences in one or more insect expression vectors, and employing an insect expression system. Materials and methods for baculovirus/insect cell expression systems are commercially available in kit form from, *e.g.*, Invitrogen, San Diego, Calif., U.S.A. (the MaxBat™ kit), and such methods are well known in the art, as described in Summers and Smith, Texas Agricultural Experiment Station Bulletin No. 1555 (1987), incorporated herein by reference. As used herein, an insect cell capable of expressing a polynucleotide of the present invention is "transformed."

The protein of the invention may be prepared by culturing transformed host cells under culture conditions suitable to express the recombinant protein. The resulting expressed protein may then be purified from such culture (*i.e.*, from culture medium or cell extracts) using known purification processes, such as gel filtration and ion exchange chromatography. The purification of the protein may also include an affinity column containing agents which will bind to the protein; one or more column steps over such affinity resins as concanavalin A-agarose, heparin-toyopearl™ or Cibacrom blue 3GA Sepharose™; one or more steps involving hydrophobic interaction chromatography using such resins as phenyl ether, butyl ether, or propyl ether; or immunoaffinity chromatography.

Alternatively, the protein of the invention may also be expressed in a form that will facilitate purification. For example, it may be expressed as a fusion protein, such as those of maltose binding protein (MBP), glutathione-S-transferase (GST) or thioredoxin (TRX), or as a His-tag. Kits for expression and purification of such fusion proteins are commercially available from New England BioLab (Beverly, Mass.), Pharmacia (Piscataway, N.J.) and Invitrogen, respectively. The protein can also be tagged with an epitope and subsequently purified by using a specific antibody directed to such epitope. One such epitope ("FLAG®") is commercially available from Kodak (New Haven, Conn.).

Finally, one or more reverse-phase high performance liquid chromatography (RP- HPLC) steps employing hydrophobic RP-HPLC media, *e.g.*, silica gel having pendant methyl or other aliphatic groups, can be employed to further purify the protein. Some or all of the foregoing purification steps, in various combinations, can also be employed to provide a substantially homogeneous isolated recombinant protein. The protein thus purified is substantially free of other mammalian proteins and is defined in accordance with the present invention as an "isolated protein."

The polypeptides of the invention include analogs (variants). This embraces fragments, as well as peptides in which one or more amino acids has been deleted, inserted, or substituted. Also, analogs of the polypeptides of the invention embrace fusions of the polypeptides or modifications of the polypeptides of the invention, wherein the polypeptide or analog is fused to another moiety or moieties, *e.g.*, targeting moiety or another therapeutic agent. Such analogs may exhibit improved properties such as activity and/or stability. Examples of moieties which may be fused to the polypeptide or an analog include, for example, targeting moieties which provide for the delivery of polypeptide to pancreatic cells, *e.g.*, antibodies to pancreatic cells, antibodies to immune cells such as T-cells, monocytes, dendritic cells, granulocytes, etc., as well as receptor and ligands expressed on pancreatic or immune cells. Other moieties which may be fused to the polypeptide include therapeutic agents which are used for treatment, for example, immunosuppressive drugs such as cyclosporin, SK506, azathioprine, CD3 antibodies and steroids. Also, polypeptides may be fused to immune modulators, and other cytokines such as alpha or beta interferon.

4.6.1 DETERMINING POLYPEPTIDE AND POLYNUCLEOTIDE IDENTITY AND SIMILARITY

Preferred identity and/or similarity are designed to give the largest match between the sequences tested. Methods to determine identity and similarity are codified in computer programs including, but are not limited to, the GCG program package, including GAP (Devereux, J., et al., Nucleic Acids Research 12(1):387 (1984); Genetics Computer Group, University of Wisconsin, Madison, WI), BLASTP, BLASTN, BLASTX, FASTA (Altschul, S.F. et al., J. Molec. Biol. 215:403-410 (1990), PSI-BLAST (Altschul S.F. et al., Nucleic Acids Res. vol. 25, pp. 3389-3402, herein incorporated by reference), eMatrix software (Wu et al., J. Comp. Biol., Vol. 6, pp. 219-235 (1999), herein incorporated by reference), eMotif software (Nevill-Manning et al, ISMB-97, Vol. 4, pp. 202-209, herein incorporated by reference), pFam software (Sonnhammer et al., Nucleic Acids Res., Vol. 26(1), pp. 320-322 (1998), herein incorporated by reference) and the Kyte-Doolittle hydrophobocity prediction algorithm (J. Mol Biol, 157, pp. 105-31 (1982), incorporated herein by reference). The BLAST programs are publicly available from the National Center for Biotechnology Information (NCBI) and other sources (BLAST Manual, Altschul, S., et al. NCB NLM NIH Bethesda, MD 20894; Altschul, S., et al., J. Mol. Biol. 215:403-410 (1990).

4.7 CHIMERIC AND FUSION PROTEINS

The invention also provides chimeric or fusion proteins. As used herein, a "chimeric protein" or "fusion protein" comprises a polypeptide of the invention operatively linked to

another polypeptide. Within a fusion protein the polypeptide according to the invention can correspond to all or a portion of a protein according to the invention. In one embodiment, a fusion protein comprises at least one biologically active portion of a protein according to the invention. In another embodiment, a fusion protein comprises at least two biologically active portions of a protein according to the invention. Within the fusion protein, the term "operatively linked" is intended to indicate that the polypeptide according to the invention and the other polypeptide are fused in-frame to each other. The polypeptide can be fused to the N-terminus or C-terminus.

For example, in one embodiment a fusion protein comprises a polypeptide according to the invention operably linked to the extracellular domain of a second protein.

In another embodiment, the fusion protein is a GST-fusion protein in which the polypeptide sequences of the invention are fused to the C-terminus of the GST (*i.e.*, glutathione S-transferase) sequences.

In another embodiment, the fusion protein is an immunoglobulin fusion protein in which the polypeptide sequences according to the invention comprises one or more domains are fused to sequences derived from a member of the immunoglobulin protein family. The immunoglobulin fusion proteins of the invention can be incorporated into pharmaceutical compositions and administered to a subject to inhibit an interaction between a ligand and a protein of the invention on the surface of a cell, to thereby suppress signal transduction *in vivo*. The immunoglobulin fusion proteins can be used to affect the bioavailability of a cognate ligand. Inhibition of the ligand/protein interaction may be useful therapeutically for both the treatment of proliferative and differentiative disorders, *e,g.,* cancer as well as modulating (*e.g.*, promoting or inhibiting) cell survival. Moreover, the immunoglobulin fusion proteins of the invention can be used as immunogens to produce antibodies in a subject, to purify ligands, and in screening assays to identify molecules that inhibit the interaction of a polypeptide of the invention with a ligand.

A chimeric or fusion protein of the invention can be produced by standard recombinant DNA techniques. For example, DNA fragments coding for the different polypeptide sequences are ligated together in-frame in accordance with conventional techniques, *e.g.*, by employing blunt-ended or stagger-ended termini for ligation, restriction enzyme digestion to provide for appropriate termini, filling-in of cohesive ends as appropriate, alkaline phosphatase treatment to avoid undesirable joining, and enzymatic ligation. In another embodiment, the fusion gene can be synthesized by conventional techniques including automated DNA synthesizers. Alternatively, PCR amplification of gene fragments can be carried out using anchor primers that give rise to complementary overhangs between two consecutive gene fragments that can subsequently be annealed and reamplified to generate a chimeric gene sequence (see, for

example, Ausubel et al. (eds.) CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, 1992). Moreover, many expression vectors are commercially available that already encode a fusion moiety (*e.g.*, a GST polypeptide). A nucleic acid encoding a polypeptide of the invention can be cloned into such an expression vector such that the fusion moiety is linked in-frame to the protein of the invention.

4.8 GENE THERAPY

Mutations in the polynucleotides of the invention gene may result in loss of normal function of the encoded protein. The invention thus provides gene therapy to restore normal activity of the polypeptides of the invention; or to treat disease states involving polypeptides of the invention. Delivery of a functional gene encoding polypeptides of the invention to appropriate cells is effected *ex vivo*, *in situ*, or *in vivo* by use of vectors, and more particularly viral vectors (*e.g.*, adenovirus, adeno-associated virus, or a retrovirus), or *ex vivo* by use of physical DNA transfer methods (*e.g.*, liposomes or chemical treatments). See, for example, Anderson, Nature, supplement to vol. 392, no. 6679, pp.25-20 (1998). For additional reviews of gene therapy technology see Friedmann, Science, 244: 1275-1281 (1989); Verma, Scientific American: 68-84 (1990); and Miller, Nature, 357: 455-460 (1992). Introduction of any one of the nucleotides of the present invention or a gene encoding the polypeptides of the present invention can also be accomplished with extrachromosomal substrates (transient expression) or artificial chromosomes (stable expression). Cells may also be cultured *ex vivo* in the presence of proteins of the present invention in order to proliferate or to produce a desired effect on or activity in such cells. Treated cells can then be introduced *in vivo* for therapeutic purposes. Alternatively, it is contemplated that in other human disease states, preventing the expression of or inhibiting the activity of polypeptides of the invention will be useful in treating the disease states. It is contemplated that antisense therapy or gene therapy could be applied to negatively regulate the expression of polypeptides of the invention.

Other methods inhibiting expression of a protein include the introduction of antisense molecules to the nucleic acids of the present invention, their complements, or their translated RNA sequences, by methods known in the art. Further, the polypeptides of the present invention can be inhibited by using targeted deletion methods, or the insertion of a negative regulatory element such as a silencer, which is tissue specific.

The present invention still further provides cells genetically engineered *in vivo* to express the polynucleotides of the invention, wherein such polynucleotides are in operative association with a regulatory sequence heterologous to the host cell which drives expression of the polynucleotides in

the cell. These methods can be used to increase or decrease the expression of the polynucleotides of the present invention.

Knowledge of DNA sequences provided by the invention allows for modification of cells to permit, increase, or decrease, expression of endogenous polypeptide. Cells can be modified (*e.g.*, by homologous recombination) to provide increased polypeptide expression by replacing, in whole or in part, the naturally occurring promoter with all or part of a heterologous promoter so that the cells express the protein at higher levels. The heterologous promoter is inserted in such a manner that it is operatively linked to the desired protein encoding sequences. See, for example, PCT International Publication No. WO 94/12650, PCT International Publication No. WO 92/20808, and PCT International Publication No. WO 91/09955. It is also contemplated that, in addition to heterologous promoter DNA, amplifiable marker DNA (*e.g.*, ada, dhfr, and the multifunctional CAD gene which encodes carbamyl phosphate synthase, aspartate transcarbamylase, and dihydroorotase) and/or intron DNA may be inserted along with the heterologous promoter DNA. If linked to the desired protein coding sequence, amplification of the marker DNA by standard selection methods results in co-amplification of the desired protein coding sequences in the cells.

In another embodiment of the present invention, cells and tissues may be engineered to express an endogenous gene comprising the polynucleotides of the invention under the control of inducible regulatory elements, in which case the regulatory sequences of the endogenous gene may be replaced by homologous recombination. As described herein, gene targeting can be used to replace a gene's existing regulatory region with a regulatory sequence isolated from a different gene or a novel regulatory sequence synthesized by genetic engineering methods. Such regulatory sequences may be comprised of promoters, enhancers, scaffold-attachment regions, negative regulatory elements, transcriptional initiation sites, regulatory protein binding sites or combinations of said sequences. Alternatively, sequences which affect the structure or stability of the RNA or protein produced may be replaced, removed, added, or otherwise modified by targeting. These sequences include polyadenylation signals, mRNA stability elements, splice sites, leader sequences for enhancing or modifying transport or secretion properties of the protein, or other sequences which alter or improve the function or stability of protein or RNA molecules.

The targeting event may be a simple insertion of the regulatory sequence, placing the gene under the control of the new regulatory sequence, *e.g.*, inserting a new promoter or enhancer or both upstream of a gene. Alternatively, the targeting event may be a simple deletion of a regulatory element, such as the deletion of a tissue-specific negative regulatory element. Alternatively, the targeting event may replace an existing element; for example, a tissue-specific enhancer can be replaced by an enhancer that has broader or different cell-type specificity than the naturally occurring elements. Here, the naturally occurring sequences are deleted and new sequences are

added. In all cases, the identification of the targeting event may be facilitated by the use of one or more selectable marker genes that are contiguous with the targeting DNA, allowing for the selection of cells in which the exogenous DNA has integrated into the cell genome. The identification of the targeting event may also be facilitated by the use of one or more marker genes exhibiting the property of negative selection, such that the negatively selectable marker is linked to the exogenous DNA, but configured such that the negatively selectable marker flanks the targeting sequence, and such that a correct homologous recombination event with sequences in the host cell genome does not result in the stable integration of the negatively selectable marker. Markers useful for this purpose include the Herpes Simplex Virus thymidine kinase (TK) gene or the bacterial xanthine-guanine phosphoribosyl-transferase (gpt) gene.

The gene targeting or gene activation techniques which can be used in accordance with this aspect of the invention are more particularly described in U.S. Patent No. 5,272,071 to Chappel; U.S. Patent No. 5,578,461 to Sherwin et al.; International Application No. PCT/US92/09627 (WO93/09222) by Selden et al.; and International Application No. PCT/US90/06436 (WO91/06667) by Skoultchi et al., each of which is incorporated by reference herein in its entirety.

4.9 TRANSGENIC ANIMALS

In preferred methods to determine biological functions of the polypeptides of the invention in vivo, one or more genes provided by the invention are either over expressed or inactivated in the germ line of animals using homologous recombination [Capecchi, Science 244:1288-1292 (1989)]. Animals in which the gene is over expressed, under the regulatory control of exogenous or endogenous promoter elements, are known as transgenic animals. Animals in which an endogenous gene has been inactivated by homologous recombination are referred to as "knockout" animals. Knockout animals, preferably non-human mammals, can be prepared as described in U.S. Patent No. 5,557,032, incorporated herein by reference. Transgenic animals are useful to determine the roles polypeptides of the invention play in biological processes, and preferably in disease states. Transgenic animals are useful as model systems to identify compounds that modulate lipid metabolism. Transgenic animals, preferably non-human mammals, are produced using methods as described in U.S. Patent No 5,489,743 and PCT Publication No. WO94/28122, incorporated herein by reference.

Transgenic animals can be prepared wherein all or part of a promoter of the polynucleotides of the invention is either activated or inactivated to alter the level of expression of the polypeptides of the invention. Inactivation can be carried out using homologous recombination methods described above. Activation can be achieved by supplementing or even replacing the homologous promoter to provide for increased protein expression. The

homologous promoter can be supplemented by insertion of one or more heterologous enhancer elements known to confer promoter activation in a particular tissue.

The polynucleotides of the present invention also make possible the development, through, *e.g.*, homologous recombination or knock out strategies, of animals that fail to express polypeptides of the invention or that express a variant polypeptide. Such animals are useful as models for studying the *in vivo* activities of polypeptide as well as for studying modulators of the polypeptides of the invention.

In preferred methods to determine biological functions of the polypeptides of the invention *in vivo*, one or more genes provided by the invention are either over expressed or inactivated in the germ line of animals using homologous recombination [Capecchi, Science 244:1288-1292 (1989)]. Animals in which the gene is over expressed, under the regulatory control of exogenous or endogenous promoter elements, are known as transgenic animals. Animals in which an endogenous gene has been inactivated by homologous recombination are referred to as "knockout" animals. Knockout animals, preferably non-human mammals, can be prepared as described in U.S. Patent No. 5,557,032, incorporated herein by reference. Transgenic animals are useful to determine the roles polypeptides of the invention play in biological processes, and preferably in disease states. Transgenic animals are useful as model systems to identify compounds that modulate lipid metabolism. Transgenic animals, preferably non-human mammals, are produced using methods as described in U.S. Patent No 5,489,743 and PCT Publication No. WO94/28122, incorporated herein by reference.

Transgenic animals can be prepared wherein all or part of the polynucleotides of the invention promoter is either activated or inactivated to alter the level of expression of the polypeptides of the invention. Inactivation can be carried out using homologous recombination methods described above. Activation can be achieved by supplementing or even replacing the homologous promoter to provide for increased protein expression. The homologous promoter can be supplemented by insertion of one or more heterologous enhancer elements known to confer promoter activation in a particular tissue.

4.10 USES AND BIOLOGICAL ACTIVITY

The polynucleotides and proteins of the present invention are expected to exhibit one or more of the uses or biological activities (including those associated with assays cited herein) identified herein. Uses or activities described for proteins of the present invention may be provided by administration or use of such proteins or of polynucleotides encoding such proteins (such as, for example, in gene therapies or vectors suitable for introduction of DNA). The mechanism underlying the particular condition or pathology will dictate whether the

polypeptides of the invention, the polynucleotides of the invention or modulators (activators or inhibitors) thereof would be beneficial to the subject in need of treatment. Thus, "therapeutic compositions of the invention" include compositions comprising isolated polynucleotides (including recombinant DNA molecules, cloned genes and degenerate variants thereof) or polypeptides of the invention (including full length protein, mature protein and truncations or domains thereof), or compounds and other substances that modulate the overall activity of the target gene products, either at the level of target gene/protein expression or target protein activity. Such modulators include polypeptides, analogs, (variants), including fragments and fusion proteins, antibodies and other binding proteins; chemical compounds that directly or indirectly activate or inhibit the polypeptides of the invention (identified, *e.g.*, via drug screening assays as described herein); antisense polynucleotides and polynucleotides suitable for triple helix formation; and in particular antibodies or other binding partners that specifically recognize one or more epitopes of the polypeptides of the invention.

The polypeptides of the present invention may likewise be involved in cellular activation or in one of the other physiological pathways described herein.

4.10.1 RESEARCH USES AND UTILITIES

The polynucleotides provided by the present invention can be used by the research community for various purposes. The polynucleotides can be used to express recombinant protein for analysis, characterization or therapeutic use; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in disease states); as molecular weight markers on gels; as chromosome markers or tags (when labeled) to identify chromosomes or to map related gene positions; to compare with endogenous DNA sequences in patients to identify potential genetic disorders; as probes to hybridize and thus discover novel, related DNA sequences; as a source of information to derive PCR primers for genetic fingerprinting; as a probe to "subtract-out" known sequences in the process of discovering other novel polynucleotides; for selecting and making oligomers for attachment to a "gene chip" or other support, including for examination of expression patterns; to raise anti-protein antibodies using DNA immunization techniques; and as an antigen to raise anti-DNA antibodies or elicit another immune response. Where the polynucleotide encodes a protein which binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the polynucleotide can also be used in interaction trap assays (such as, for example, that described in Gyuris et al., Cell 75:791-803 (1993)) to identify polynucleotides encoding the other protein with which binding occurs or to identify inhibitors of the binding interaction.

The polypeptides provided by the present invention can similarly be used in assays to determine biological activity, including in a panel of multiple proteins for high-throughput screening; to raise antibodies or to elicit another immune response; as a reagent (including the labeled reagent) in assays designed to quantitatively determine levels of the protein (or its receptor) in biological fluids; as markers for tissues in which the corresponding polypeptide is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in a disease state); and, of course, to isolate correlative receptors or ligands. Proteins involved in these binding interactions can also be used to screen for peptide or small molecule inhibitors or agonists of the binding interaction.

Any or all of these research utilities are capable of being developed into reagent grade or kit format for commercialization as research products.

Methods for performing the uses listed above are well known to those skilled in the art. References disclosing such methods include without limitation "Molecular Cloning: A Laboratory Manual", 2d ed., Cold Spring Harbor Laboratory Press, Sambrook, J., E. F. Fritsch and T. Maniatis eds., 1989, and "Methods in Enzymology: Guide to Molecular Cloning Techniques", Academic Press, Berger, S. L. and A. R. Kimmel eds., 1987.

4.10.2 NUTRITIONAL USES

Polynucleotides and polypeptides of the present invention can also be used as nutritional sources or supplements. Such uses include without limitation use as a protein or amino acid supplement, use as a carbon source, use as a nitrogen source and use as a source of carbohydrate. In such cases the polypeptide or polynucleotide of the invention can be added to the feed of a particular organism or can be administered as a separate solid or liquid preparation, such as in the form of powder, pills, solutions, suspensions or capsules. In the case of microorganisms, the polypeptide or polynucleotide of the invention can be added to the medium in or on which the microorganism is cultured.

4.10.3 CYTOKINE AND CELL PROLIFERATION/DIFFERENTIATION ACTIVITY

A polypeptide of the present invention may exhibit activity relating to cytokine, cell proliferation (either inducing or inhibiting) or cell differentiation (either inducing or inhibiting) activity or may induce production of other cytokines in certain cell populations. A polynucleotide of the invention can encode a polypeptide exhibiting such attributes. Many protein factors discovered to date, including all known cytokines, have exhibited activity in one or more factor-dependent cell proliferation assays, and hence the assays serve as a convenient

confirmation of cytokine activity. The activity of therapeutic compositions of the present invention is evidenced by any one of a number of routine factor dependent cell proliferation assays for cell lines including, without limitation, 32D, DA2, DA1G, T10, B9, B9/11, BaF3, MC9/G, M+(preB M+), 2E8, RB5, DA1, 123, T1165, HT2, CTLL2, TF-1, Mo7e, CMK, HUVEC, and Caco. Therapeutic compositions of the invention can be used in the following:

Assays for T-cell or thymocyte proliferation include without limitation those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A. M. Kruisbeek, D. H. Margulies, E. M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, *In Vitro* assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Bertagnolli et al., J. Immunol. 145:1706-1712, 1990; Bertagnolli et al., Cellular Immunology 133:327-341, 1991; Bertagnolli, et al., I. Immunol. 149:3778-3783, 1992; Bowman et al., I. Immunol. 152:1756-1761, 1994.

Assays for cytokine production and/or proliferation of spleen cells, lymph node cells or thymocytes include, without limitation, those described in: Polyclonal T cell stimulation, Kruisbeek, A. M. and Shevach, E. M. In Current Protocols in Immunology. J. E. e.a. Coligan eds. Vol 1 pp. 3.12.1-3.12.14, John Wiley and Sons, Toronto. 1994; and Measurement of mouse and human interleukin-γ, Schreiber, R. D. In Current Protocols in Immunology. J. E. e.a. Coligan eds. Vol 1 pp. 6.8.1-6.8.8, John Wiley and Sons, Toronto. 1994.

Assays for proliferation and differentiation of hematopoietic and lymphopoietic cells include, without limitation, those described in: Measurement of Human and Murine Interleukin 2 and Interleukin 4, Bottomly, K., Davis, L. S. and Lipsky, P. E. In Current Protocols in Immunology. J. E. e.a. Coligan eds. Vol 1 pp. 6.3.1-6.3.12, John Wiley and Sons, Toronto. 1991; deVries et al., J. Exp. Med. 173:1205-1211, 1991; Moreau et al., Nature 336:690-692, 1988; Greenberger et al., Proc. Natl. Acad. Sci. U.S.A. 80:2931-2938, 1983; Measurement of mouse and human interleukin 6--Nordan, R. In Current Protocols in Immunology. J. E. Coligan eds. Vol 1 pp. 6.6.1-6.6.5, John Wiley and Sons, Toronto. 1991; Smith et al., Proc. Natl. Aced. Sci. U.S.A. 83:1857-1861, 1986; Measurement of human Interleukin 11--Bennett, F., Giannotti, J., Clark, S. C. and Turner, K. J. In Current Protocols in Immunology. J. E. Coligan eds. Vol 1 pp. 6.15.1 John Wiley and Sons, Toronto. 1991; Measurement of mouse and human Interleukin 9--Ciarletta, A., Giannotti, J., Clark, S. C. and Turner, K. J. In Current Protocols in Immunology. J. E. Coligan eds. Vol 1 pp. 6.13.1, John Wiley and Sons, Toronto. 1991.

Assays for T-cell clone responses to antigens (which will identify, among others, proteins that affect APC-T cell interactions as well as direct T-cell effects by measuring proliferation and cytokine production) include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A. M. Kruisbeek, D. H. Margulies, E. M. Shevach, W Strober,

Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, *In Vitro* assays for Mouse Lymphocyte Function; Chapter 6, Cytokines and their cellular receptors; Chapter 7, Immunologic studies in Humans); Weinberger et al., Proc. Natl. Acad. Sci. USA 77:6091-6095, 1980; Weinberger et al., Eur. J. Immun. 11:405-411, 1981; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988.

4.10.4 STEM CELL GROWTH FACTOR ACTIVITY

A polypeptide of the present invention may exhibit stem cell growth factor activity and be involved in the proliferation, differentiation and survival of pluripotent and totipotent stem cells including primordial germ cells, embryonic stem cells, hematopoietic stem cells and/or germ line stem cells. Administration of the polypeptide of the invention to stem cells *in vivo* or *ex vivo* is expected to maintain and expand cell populations in a totipotential or pluripotential state which would be useful for re-engineering damaged or diseased tissues, transplantation, manufacture of bio-pharmaceuticals and the development of bio-sensors. The ability to produce large quantities of human cells has important working applications for the production of human proteins which currently must be obtained from non-human sources or donors, implantation of cells to treat diseases such as Parkinson's, Alzheimer's and other neurodegenerative diseases; tissues for grafting such as bone marrow, skin, cartilage, tendons, bone, muscle (including cardiac muscle), blood vessels, cornea, neural cells, gastrointestinal cells and others; and organs for transplantation such as kidney, liver, pancreas (including islet cells), heart and lung.

It is contemplated that multiple different exogenous growth factors and/or cytokines may be administered in combination with the polypeptide of the invention to achieve the desired effect, including any of the growth factors listed herein, other stem cell maintenance factors, and specifically including stem cell factor (SCF), leukemia inhibitory factor (LIF), Flt-3 ligand (Flt-3L), any of the interleukins, recombinant soluble IL-6 receptor fused to IL-6, macrophage inflammatory protein 1-alpha (MIP-1-alpha), G-CSF, GM-CSF, thrombopoietin (TPO), platelet factor 4 (PF-4), platelet-derived growth factor (PDGF), neural growth factors and basic fibroblast growth factor (bFGF).

Since totipotent stem cells can give rise to virtually any mature cell type, expansion of these cells in culture will facilitate the production of large quantities of mature cells. Techniques for culturing stem cells are known in the art and administration of polypeptides of the invention, optionally with other growth factors and/or cytokines, is expected to enhance the survival and proliferation of the stem cell populations. This can be accomplished by direct administration of the polypeptide of the invention to the culture medium. Alternatively, stroma cells transfected with a polynucleotide that encodes for the polypeptide of the invention can be used as a feeder

layer for the stem cell populations in culture or in vivo. Stromal support cells for feeder layers may include embryonic bone marrow fibroblasts, bone marrow stromal cells, fetal liver cells, or cultured embryonic fibroblasts (see U.S. Patent No. 5,690,926).

Stem cells themselves can be transfected with a polynucleotide of the invention to induce autocrine expression of the polypeptide of the invention. This will allow for generation of undifferentiated totipotential/pluripotential stem cell lines that are useful as is or that can then be differentiated into the desired mature cell types. These stable cell lines can also serve as a source of undifferentiated totipotential/pluripotential mRNA to create cDNA libraries and templates for polymerase chain reaction experiments. These studies would allow for the isolation and identification of differentially expressed genes in stem cell populations that regulate stem cell proliferation and/or maintenance.

Expansion and maintenance of totipotent stem cell populations will be useful in the treatment of many pathological conditions. For example, polypeptides of the present invention may be used to manipulate stem cells in culture to give rise to neuroepithelial cells that can be used to augment or replace cells damaged by illness, autoimmune disease, accidental damage or genetic disorders. The polypeptide of the invention may be useful for inducing the proliferation of neural cells and for the regeneration of nerve and brain tissue, *i.e.* for the treatment of central and peripheral nervous system diseases and neuropathies, as well as mechanical and traumatic disorders which involve degeneration, death or trauma to neural cells or nerve tissue. In addition, the expanded stem cell populations can also be genetically altered for gene therapy purposes and to decrease host rejection of replacement tissues after grafting or implantation.

Expression of the polypeptide of the invention and its effect on stem cells can also be manipulated to achieve controlled differentiation of the stem cells into more differentiated cell types. A broadly applicable method of obtaining pure populations of a specific differentiated cell type from undifferentiated stem cell populations involves the use of a cell-type specific promoter driving a selectable marker. The selectable marker allows only cells of the desired type to survive. For example, stem cells can be induced to differentiate into cardiomyocytes (Wobus et al., Differentiation, 48: 173-182, (1991); Klug et al., J. Clin. Invest., 98(1): 216-224, (1998)) or skeletal muscle cells (Browder, L. W. In: *Principles of Tissue Engineering eds.* Lanza et al., Academic Press (1997)). Alternatively, directed differentiation of stem cells can be accomplished by culturing the stem cells in the presence of a differentiation factor such as retinoic acid and an antagonist of the polypeptide of the invention which would inhibit the effects of endogenous stem cell factor activity and allow differentiation to proceed.

In vitro cultures of stem cells can be used to determine if the polypeptide of the invention exhibits stem cell growth factor activity. Stem cells are isolated from any one of various cell

sources (including hematopoietic stem cells and embryonic stem cells) and cultured on a feeder layer, as described by Thompson et al. Proc. Natl. Acad. Sci, U.S.A., 92: 7844-7848 (1995), in the presence of the polypeptide of the invention alone or in combination with other growth factors or cytokines. The ability of the polypeptide of the invention to induce stem cells proliferation is determined by colony formation on semi-solid support *e.g.* as described by Bernstein et al., Blood, 77: 2316-2321 (1991).

4.10.5 HEMATOPOIESIS REGULATING ACTIVITY

A polypeptide of the present invention may be involved in regulation of hematopoiesis and, consequently, in the treatment of myeloid or lymphoid cell disorders. Even marginal biological activity in support of colony forming cells or of factor-dependent cell lines indicates involvement in regulating hematopoiesis, *e.g.* in supporting the growth and proliferation of erythroid progenitor cells alone or in combination with other cytokines, thereby indicating utility, for example, in treating various anemias or for use in conjunction with irradiation/chemotherapy to stimulate the production of erythroid precursors and/or erythroid cells; in supporting the growth and proliferation of myeloid cells such as granulocytes and monocytes/macrophages (*i.e.*, traditional CSF activity) useful, for example, in conjunction with chemotherapy to prevent or treat consequent myelo-suppression; in supporting the growth and proliferation of megakaryocytes and consequently of platelets thereby allowing prevention or treatment of various platelet disorders such as thrombocytopenia, and generally for use in place of or complimentary to platelet transfusions; and/or in supporting the growth and proliferation of hematopoietic stem cells which are capable of maturing to any and all of the above-mentioned hematopoietic cells and therefore find therapeutic utility in various stem cell disorders (such as those usually treated with transplantation, including, without limitation, aplastic anemia and paroxysmal nocturnal hemoglobinuria), as well as in repopulating the stem cell compartment post irradiation/chemotherapy, either *in-vivo* or *ex-vivo* (*i.e.*, in conjunction with bone marrow transplantation or with peripheral progenitor cell transplantation (homologous or heterologous)) as normal cells or genetically manipulated for gene therapy.

Therapeutic compositions of the invention can be used in the following:

Suitable assays for proliferation and differentiation of various hematopoietic lines are cited above.

Assays for embryonic stem cell differentiation (which will identify, among others, proteins that influence embryonic differentiation hematopoiesis) include, without limitation, those described in: Johansson et al. Cellular Biology 15:141-151, 1995; Keller et al., Molecular and Cellular Biology 13:473-486, 1993; McClanahan et al., Blood 81:2903-2915, 1993.

Assays for stem cell survival and differentiation (which will identify, among others, proteins that regulate lympho-hematopoiesis) include, without limitation, those described in: Methylcellulose colony forming assays, Freshney, M. G. In Culture of Hematopoietic Cells. R. I. Freshney, et al. eds. Vol pp. 265-268, Wiley-Liss, Inc., New York, N.Y. 1994; Hirayama et al., Proc. Natl. Acad. Sci. USA 89:5907-5911, 1992; Primitive hematopoietic colony forming cells with high proliferative potential, McNiece, I. K. and Briddell, R. A. In Culture of Hematopoietic Cells. R. I. Freshney, et al. eds. Vol pp. 23-39, Wiley-Liss, Inc., New York, N.Y. 1994; Neben et al., Experimental Hematology 22:353-359, 1994; Cobblestone area forming cell assay, Ploemacher, R. E. In Culture of Hematopoietic Cells. R. I. Freshney, et al. eds. Vol pp. 1-21, Wiley-Liss, Inc., New York, N.Y. 1994; Long term bone marrow cultures in the presence of stromal cells, Spooncer, E., Dexter, M. and Allen, T. In Culture of Hematopoietic Cells. R. I. Freshney, et al. eds. Vol pp. 163-179, Wiley-Liss, Inc., New York, N.Y. 1994; Long term culture initiating cell assay, Sutherland, H. J. In Culture of Hematopoietic Cells. R. I. Freshney, et al. eds. Vol pp. 139-162, Wiley-Liss, Inc., New York, N.Y. 1994.

4.10.6 TISSUE GROWTH ACTIVITY

A polypeptide of the present invention also may be involved in bone, cartilage, tendon, ligament and/or nerve tissue growth or regeneration, as well as in wound healing and tissue repair and replacement, and in healing of burns, incisions and ulcers.

A polypeptide of the present invention which induces cartilage and/or bone growth in circumstances where bone is not normally formed, has application in the healing of bone fractures and cartilage damage or defects in humans and other animals. Compositions of a polypeptide, antibody, binding partner, or other modulator of the invention may have prophylactic use in closed as well as open fracture reduction and also in the improved fixation of artificial joints. De novo bone formation induced by an osteogenic agent contributes to the repair of congenital, trauma induced, or oncologic resection induced craniofacial defects, and also is useful in cosmetic plastic surgery.

A polypeptide of this invention may also be involved in attracting bone-forming cells, stimulating growth of bone-forming cells, or inducing differentiation of progenitors of bone-forming cells. Treatment of osteoporosis, osteoarthritis, bone degenerative disorders, or periodontal disease, such as through stimulation of bone and/or cartilage repair or by blocking inflammation or processes of tissue destruction (collagenase activity, osteoclast activity, etc.) mediated by inflammatory processes may also be possible using the composition of the invention.

Another category of tissue regeneration activity that may involve the polypeptide of the present invention is tendon/ligament formation. Induction of tendon/ligament-like tissue or other tissue formation in circumstances where such tissue is not normally formed, has application in the healing of tendon or ligament tears, deformities and other tendon or ligament defects in humans and other animals. Such a preparation employing a tendon/ligament-like tissue inducing protein may have prophylactic use in preventing damage to tendon or ligament tissue, as well as use in the improved fixation of tendon or ligament to bone or other tissues, and in repairing defects to tendon or ligament tissue. De novo tendon/ligament-like tissue formation induced by a composition of the present invention contributes to the repair of congenital, trauma induced, or other tendon or ligament defects of other origin, and is also useful in cosmetic plastic surgery for attachment or repair of tendons or ligaments. The compositions of the present invention may provide environment to attract tendon- or ligament-forming cells, stimulate growth of tendon- or ligament-forming cells, induce differentiation of progenitors of tendon- or ligament-forming cells, or induce growth of tendon/ligament cells or progenitors *ex vivo* for return *in vivo* to effect tissue repair. The compositions of the invention may also be useful in the treatment of tendinitis, carpal tunnel syndrome and other tendon or ligament defects. The compositions may also include an appropriate matrix and/or sequestering agent as a carrier as is well known in the art.

The compositions of the present invention may also be useful for proliferation of neural cells and for regeneration of nerve and brain tissue, *i.e.* for the treatment of central and peripheral nervous system diseases and neuropathies, as well as mechanical and traumatic disorders, which involve degeneration, death or trauma to neural cells or nerve tissue. More specifically, a composition may be used in the treatment of diseases of the peripheral nervous system, such as peripheral nerve injuries, peripheral neuropathy and localized neuropathies, and central nervous system diseases, such as Alzheimer's, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and Shy-Drager syndrome. Further conditions that may be treated in accordance with the present invention include mechanical and traumatic disorders, such as spinal cord disorders, head trauma and cerebrovascular diseases such as stroke. Peripheral neuropathies resulting from chemotherapy or other medical therapies may also be treatable using a composition of the invention.

Compositions of the invention may also be useful to promote better or faster closure of non-healing wounds, including without limitation pressure ulcers, ulcers associated with vascular insufficiency, surgical and traumatic wounds, and the like.

Compositions of the present invention may also be involved in the generation or regeneration of other tissues, such as organs (including, for example, pancreas, liver, intestine,

kidney, skin, endothelium), muscle (smooth, skeletal or cardiac) and vascular (including vascular endothelium) tissue, or for promoting the growth of cells comprising such tissues. Part of the desired effects may be by inhibition or modulation of fibrotic scarring may allow normal tissue to regenerate. A polypeptide of the present invention may also exhibit angiogenic activity.

A composition of the present invention may also be useful for gut protection or regeneration and treatment of lung or liver fibrosis, reperfusion injury in various tissues, and conditions resulting from systemic cytokine damage.

A composition of the present invention may also be useful for promoting or inhibiting differentiation of tissues described above from precursor tissues or cells; or for inhibiting the growth of tissues described above.

Therapeutic compositions of the invention can be used in the following:

Assays for tissue generation activity include, without limitation, those described in: International Patent Publication No. WO95/16035 (bone, cartilage, tendon); International Patent Publication No. WO95/05846 (nerve, neuronal); International Patent Publication No. WO91/07491 (skin, endothelium).

Assays for wound healing activity include, without limitation, those described in: Winter, Epidermal Wound Healing, pps. 71-112 (Maibach, H. I. and Rovee, D. T., eds.), Year Book Medical Publishers, Inc., Chicago, as modified by Eaglstein and Mertz, J. Invest. Dermatol 71:382-84 (1978).

4.10.7 IMMUNE STIMULATING OR SUPPRESSING ACTIVITY

A polypeptide of the present invention may also exhibit immune stimulating or immune suppressing activity, including without limitation the activities for which assays are described herein. A polynucleotide of the invention can encode a polypeptide exhibiting such activities. A protein may be useful in the treatment of various immune deficiencies and disorders (including severe combined immunodeficiency (SCID)), *e.g.*, in regulating (up or down) growth and proliferation of T and/or B lymphocytes, as well as effecting the cytolytic activity of NK cells and other cell populations. These immune deficiencies may be genetic or be caused by viral (*e.g.*, HIV) as well as bacterial or fungal infections, or may result from autoimmune disorders. More specifically, infectious diseases causes by viral, bacterial, fungal or other infection may be treatable using a protein of the present invention, including infections by HIV, hepatitis viruses, herpes viruses, mycobacteria, Leishmania spp., malaria spp. and various fungal infections such as candidiasis. Of course, in this regard, proteins of the present invention may also be useful where a boost to the immune system generally may be desirable, *i.e.*, in the treatment of cancer.

Autoimmune disorders which may be treated using a protein of the present invention include, for example, connective tissue disease, multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, autoimmune pulmonary inflammation, Guillain-Barre syndrome, autoimmune thyroiditis, insulin dependent diabetes mellitis, myasthenia gravis, graft-versus-host disease and autoimmune inflammatory eye disease. Such a protein (or antagonists thereof, including antibodies) of the present invention may also to be useful in the treatment of allergic reactions and conditions (*e.g.*, anaphylaxis, serum sickness, drug reactions, food allergies, insect venom allergies, mastocytosis, allergic rhinitis, hypersensitivity pneumonitis, urticaria, angioedema, eczema, atopic dermatitis, allergic contact dermatitis, erythema multiforme, Stevens-Johnson syndrome, allergic conjunctivitis, atopic keratoconjunctivitis, venereal keratoconjunctivitis, giant papillary conjunctivitis and contact allergies), such as asthma (particularly allergic asthma) or other respiratory problems. Other conditions, in which immune suppression is desired (including, for example, organ transplantation), may also be treatable using a protein (or antagonists thereof) of the present invention. The therapeutic effects of the polypeptides or antagonists thereof on allergic reactions can be evaluated by in vivo animals models such as the cumulative contact enhancement test (Lastbom et al., Toxicology 125: 59-66, 1998), skin prick test (Hoffmann et al., Allergy 54: 446-54, 1999), guinea pig skin sensitization test (Vohr et al., Arch. Toxocol. 73: 501-9), and murine local lymph node assay (Kimber et al., J. Toxicol. Environ. Health 53: 563-79).

Using the proteins of the invention it may also be possible to modulate immune responses, in a number of ways. Down regulation may be in the form of inhibiting or blocking an immune response already in progress or may involve preventing the induction of an immune response. The functions of activated T cells may be inhibited by suppressing T cell responses or by inducing specific tolerance in T cells, or both. Immunosuppression of T cell responses is generally an active, non-antigen-specific, process which requires continuous exposure of the T cells to the suppressive agent. Tolerance, which involves inducing non-responsiveness or anergy in T cells, is distinguishable from immunosuppression in that it is generally antigen-specific and persists after exposure to the tolerizing agent has ceased. Operationally, tolerance can be demonstrated by the lack of a T cell response upon reexposure to specific antigen in the absence of the tolerizing agent.

Down regulating or preventing one or more antigen functions (including without limitation B lymphocyte antigen functions (such as, for example, B7)), *e.g.*, preventing high level lymphokine synthesis by activated T cells, will be useful in situations of tissue, skin and organ transplantation and in graft-versus-host disease (GVHD). For example, blockage of T cell function should result in reduced tissue destruction in tissue transplantation. Typically, in tissue

transplants, rejection of the transplant is initiated through its recognition as foreign by T cells, followed by an immune reaction that destroys the transplant. The administration of a therapeutic composition of the invention may prevent cytokine synthesis by immune cells, such as T cells, and thus acts as an immunosuppressant. Moreover, a lack of costimulation may also be sufficient to anergize the T cells, thereby inducing tolerance in a subject. Induction of long-term tolerance by B lymphocyte antigen-blocking reagents may avoid the necessity of repeated administration of these blocking reagents. To achieve sufficient immunosuppression or tolerance in a subject, it may also be necessary to block the function of a combination of B lymphocyte antigens.

The efficacy of particular therapeutic compositions in preventing organ transplant rejection or GVHD can be assessed using animal models that are predictive of efficacy in humans. Examples of appropriate systems which can be used include allogeneic cardiac grafts in rats and xenogeneic pancreatic islet cell grafts in mice, both of which have been used to examine the immunosuppressive effects of CTLA4Ig fusion proteins in vivo as described in Lenschow et al., Science 257:789-792 (1992) and Turka et al., Proc. Natl. Acad. Sci USA, 89:11102-11105 (1992). In addition, murine models of GVHD (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 846-847) can be used to determine the effect of therapeutic compositions of the invention on the development of that disease.

Blocking antigen function may also be therapeutically useful for treating autoimmune diseases. Many autoimmune disorders are the result of inappropriate activation of T cells that are reactive against self-tissue and which promote the production of cytokines and autoantibodies involved in the pathology of the diseases. Preventing the activation of autoreactive T cells may reduce or eliminate disease symptoms. Administration of reagents which block stimulation of T cells can be used to inhibit T cell activation and prevent production of autoantibodies or T cell-derived cytokines which may be involved in the disease process. Additionally, blocking reagents may induce antigen-specific tolerance of autoreactive T cells which could lead to long-term relief from the disease. The efficacy of blocking reagents in preventing or alleviating autoimmune disorders can be determined using a number of well-characterized animal models of human autoimmune diseases. Examples include murine experimental autoimmune encephalitis, systemic lupus erythmatosis in MRL/lpr/lpr mice or NZB hybrid mice, murine autoimmune collagen arthritis, diabetes mellitus in NOD mice and BB rats, and murine experimental myasthenia gravis (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 840-856).

Upregulation of an antigen function (*e.g.*, a B lymphocyte antigen function), as a means of up regulating immune responses, may also be useful in therapy. Upregulation of immune

responses may be in the form of enhancing an existing immune response or eliciting an initial immune response. For example, enhancing an immune response may be useful in cases of viral infection, including systemic viral diseases such as influenza, the common cold, and encephalitis.

Alternatively, anti-viral immune responses may be enhanced in an infected patient by removing T cells from the patient, costimulating the T cells in vitro with viral antigen-pulsed APCs either expressing a peptide of the present invention or together with a stimulatory form of a soluble peptide of the present invention and reintroducing the in vitro activated T cells into the patient. Another method of enhancing anti-viral immune responses would be to isolate infected cells from a patient, transfect them with a nucleic acid encoding a protein of the present invention as described herein such that the cells express all or a portion of the protein on their surface, and reintroduce the transfected cells into the patient. The infected cells would now be capable of delivering a costimulatory signal to, and thereby activate, T cells in vivo.

A polypeptide of the present invention may provide the necessary stimulation signal to T cells to induce a T cell mediated immune response against the transfected tumor cells. In addition, tumor cells which lack MHC class I or MHC class II molecules, or which fail to reexpress sufficient mounts of MHC class I or MHC class II molecules, can be transfected with nucleic acid encoding all or a portion of (*e.g.*, a cytoplasmic-domain truncated portion) of an MHC class I alpha chain protein and β_2 microglobulin protein or an MHC class II alpha chain protein and an MHC class II beta chain protein to thereby express MHC class I or MHC class II proteins on the cell surface. Expression of the appropriate class I or class II MHC in conjunction with a peptide having the activity of a B lymphocyte antigen (*e.g.*, B7-1, B7-2, B7-3) induces a T cell mediated immune response against the transfected tumor cell. Optionally, a gene encoding an antisense construct which blocks expression of an MHC class II associated protein, such as the invariant chain, can also be cotransfected with a DNA encoding a peptide having the activity of a B lymphocyte antigen to promote presentation of tumor associated antigens and induce tumor specific immunity. Thus, the induction of a T cell mediated immune response in a human subject may be sufficient to overcome tumor-specific tolerance in the subject.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for thymocyte or splenocyte cytotoxicity include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A. M. Kruisbeek, D. H. Margulies, E. M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Herrmann et al., Proc. Natl. Acad. Sci. USA

78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., I. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Bowman et al., J. Virology 61:1992-1998; Bertagnolli et al., Cellular Immunology 133:327-341, 1991; Brown et al., J. Immunol. 153:3079-3092, 1994.

Assays for T-cell-dependent immunoglobulin responses and isotype switching (which will identify, among others, proteins that modulate T-cell dependent antibody responses and that affect Th1/Th2 profiles) include, without limitation, those described in: Maliszewski, J. Immunol. 144:3028-3033, 1990; and Assays for B cell function: In vitro antibody production, Mond, J. J. and Brunswick, M. In Current Protocols in Immunology. J. E. e.a. Coligan eds. Vol 1 pp. 3.8.1-3.8.16, John Wiley and Sons, Toronto. 1994.

Mixed lymphocyte reaction (MLR) assays (which will identify, among others, proteins that generate predominantly Th1 and CTL responses) include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A. M. Kruisbeek, D. H. Margulies, E. M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., J. Immunol. 149:3778-3783, 1992.

Dendritic cell-dependent assays (which will identify, among others, proteins expressed by dendritic cells that activate naive T-cells) include, without limitation, those described in: Guery et al., J. Immunol. 134:536-544, 1995; Inaba et al., Journal of Experimental Medicine 173:549-559, 1991; Macatonia et al., Journal of Immunology 154:5071-5079, 1995; Porgador et al., Journal of Experimental Medicine 182:255-260, 1995; Nair et al., Journal of Virology 67:4062-4069, 1993; Huang et al., Science 264:961-965, 1994; Macatonia et al., Journal of Experimental Medicine 169:1255-1264, 1989; Bhardwaj et al., Journal of Clinical Investigation 94:797-807, 1994; and Inaba et al., Journal of Experimental Medicine 172:631-640, 1990.

Assays for lymphocyte survival/apoptosis (which will identify, among others, proteins that prevent apoptosis after superantigen induction and proteins that regulate lymphocyte homeostasis) include, without limitation, those described in: Darzynkiewicz et al., Cytometry 13:795-808, 1992; Gorczyca et al., Leukemia 7:659-670, 1993; Gorczyca et al., Cancer Research 53:1945-1951, 1993; Itoh et al., Cell 66:233-243, 1991; Zacharchuk, Journal of Immunology 145:4037-4045, 1990; Zamai et al., Cytometry 14:891-897, 1993; Gorczyca et al., International Journal of Oncology 1:639-648, 1992.

Assays for proteins that influence early steps of T-cell commitment and development include, without limitation, those described in: Antica et al., Blood 84:111-117, 1994; Fine et

al., Cellular Immunology 155:111-122, 1994; Galy et al., Blood 85:2770-2778, 1995; Toki et al., Proc. Nat. Acad Sci. USA 88:7548-7551, 1991.

4.10.8 ACTIVIN/INHIBIN ACTIVITY

A polypeptide of the present invention may also exhibit activin- or inhibin-related activities. A polynucleotide of the invention may encode a polypeptide exhibiting such characteristics. Inhibins are characterized by their ability to inhibit the release of follicle stimulating hormone (FSH), while activins and are characterized by their ability to stimulate the release of follicle stimulating hormone (FSH). Thus, a polypeptide of the present invention, alone or in heterodimers with a member of the inhibin family, may be useful as a contraceptive based on the ability of inhibins to decrease fertility in female mammals and decrease spermatogenesis in male mammals. Administration of sufficient amounts of other inhibins can induce infertility in these mammals. Alternatively, the polypeptide of the invention, as a homodimer or as a heterodimer with other protein subunits of the inhibin group, may be useful as a fertility inducing therapeutic, based upon the ability of activin molecules in stimulating FSH release from cells of the anterior pituitary. See, for example, U.S. Pat. No. 4,798,885. A polypeptide of the invention may also be useful for advancement of the onset of fertility in sexually immature mammals, so as to increase the lifetime reproductive performance of domestic animals such as, but not limited to, cows, sheep and pigs.

The activity of a polypeptide of the invention may, among other means, be measured by the following methods.

Assays for activin/inhibin activity include, without limitation, those described in: Vale et al., Endocrinology 91:562-572, 1972; Ling et al., Nature 321:779-782, 1986; Vale et al., Nature 321:776-779, 1986; Mason et al., Nature 318:659-663, 1985; Forage et al., Proc. Natl. Acad. Sci. USA 83:3091-3095, 1986.

4.10.9 CHEMOTACTIC/CHEMOKINETIC ACTIVITY

A polypeptide of the present invention may be involved in chemotactic or chemokinetic activity for mammalian cells, including, for example, monocytes, fibroblasts, neutrophils, T-cells, mast cells, eosinophils, epithelial and/or endothelial cells. A polynucleotide of the invention can encode a polypeptide exhibiting such attributes. Chemotactic and chemokinetic receptor activation can be used to mobilize or attract a desired cell population to a desired site of action. Chemotactic or chemokinetic compositions (*e.g.* proteins, antibodies, binding partners, or modulators of the invention) provide particular advantages in treatment of wounds and other trauma to tissues, as well as in treatment of localized infections. For example, attraction of

lymphocytes, monocytes or neutrophils to tumors or sites of infection may result in improved immune responses against the tumor or infecting agent.

A protein or peptide has chemotactic activity for a particular cell population if it can stimulate, directly or indirectly, the directed orientation or movement of such cell population. Preferably, the protein or peptide has the ability to directly stimulate directed movement of cells. Whether a particular protein has chemotactic activity for a population of cells can be readily determined by employing such protein or peptide in any known assay for cell chemotaxis.

Therapeutic compositions of the invention can be used in the following:

Assays for chemotactic activity (which will identify proteins that induce or prevent chemotaxis) consist of assays that measure the ability of a protein to induce the migration of cells across a membrane as well as the ability of a protein to induce the adhesion of one cell population to another cell population. Suitable assays for movement and adhesion include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A. M. Kruisbeek, D. H. Marguiles, E. M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 6.12, Measurement of alpha and beta Chemokines 6.12.1-6.12.28; Taub et al. J. Clin. Invest. 95:1370-1376, 1995; Lind et al. APMIS 103:140-146, 1995; Muller et al Eur. J. Immunol. 25:1744-1748; Gruber et al. J. of Immunol. 152:5860-5867, 1994; Johnston et al. J. of Immunol. 153:1762-1768, 1994.

4.10.10 HEMOSTATIC AND THROMBOLYTIC ACTIVITY

A polypeptide of the invention may also be involved in hemostatis or thrombolysis or thrombosis. A polynucleotide of the invention can encode a polypeptide exhibiting such attributes. Compositions may be useful in treatment of various coagulation disorders (including hereditary disorders, such as hemophilias) or to enhance coagulation and other hemostatic events in treating wounds resulting from trauma, surgery or other causes. A composition of the invention may also be useful for dissolving or inhibiting formation of thromboses and for treatment and prevention of conditions resulting therefrom (such as, for example, infarction of cardiac and central nervous system vessels (*e.g.*, stroke).

Therapeutic compositions of the invention can be used in the following:

Assay for hemostatic and thrombolytic activity include, without limitation, those described in: Linet et al., J. Clin. Pharmacol. 26:131-140, 1986; Burdick et al., Thrombosis Res. 45:413-419, 1987; Humphrey et al., Fibrinolysis 5:71-79 (1991); Schaub, Prostaglandins 35:467-474, 1988.

4.10.11 CANCER DIAGNOSIS AND THERAPY

Polypeptides of the invention may be involved in cancer cell generation, proliferation or metastasis. Detection of the presence or amount of polynucleotides or polypeptides of the invention may be useful for the diagnosis and/or prognosis of one or more types of cancer. For example, the presence or increased expression of a polynucleotide/polypeptide of the invention may indicate a hereditary risk of cancer, a precancerous condition, or an ongoing malignancy. Conversely, a defect in the gene or absence of the polypeptide may be associated with a cancer condition. Identification of single nucleotide polymorphisms associated with cancer or a predisposition to cancer may also be useful for diagnosis or prognosis.

Cancer treatments promote tumor regression by inhibiting tumor cell proliferation, inhibiting angiogenesis (growth of new blood vessels that is necessary to support tumor growth) and/or prohibiting metastasis by reducing tumor cell motility or invasiveness. Therapeutic compositions of the invention may be effective in adult and pediatric oncology including in solid phase tumors/malignancies, locally advanced tumors, human soft tissue sarcomas, metastatic cancer, including lymphatic metastases, blood cell malignancies including multiple myeloma, acute and chronic leukemias, and lymphomas, head and neck cancers including mouth cancer, larynx cancer and thyroid cancer, lung cancers including small cell carcinoma and non-small cell cancers, breast cancers including small cell carcinoma and ductal carcinoma, gastrointestinal cancers including esophageal cancer, stomach cancer, colon cancer, colorectal cancer and polyps associated with colorectal neoplasia, pancreatic cancers, liver cancer, urologic cancers including bladder cancer and prostate cancer, malignancies of the female genital tract including ovarian carcinoma, uterine (including endometrial) cancers, and solid tumor in the ovarian follicle, kidney cancers including renal cell carcinoma, brain cancers including intrinsic brain tumors, neuroblastoma, astrocytic brain tumors, gliomas, metastatic tumor cell invasion in the central nervous system, bone cancers including osteomas, skin cancers including malignant melanoma, tumor progression of human skin keratinocytes, squamous cell carcinoma, basal cell carcinoma, hemangiopericytoma and Karposi's sarcoma.

Polypeptides, polynucleotides, or modulators of polypeptides of the invention (including inhibitors and stimulators of the biological activity of the polypeptide of the invention) may be administered to treat cancer. Therapeutic compositions can be administered in therapeutically effective dosages alone or in combination with adjuvant cancer therapy such as surgery, chemotherapy, radiotherapy, thermotherapy, and laser therapy, and may provide a beneficial effect, *e.g.* reducing tumor size, slowing rate of tumor growth, inhibiting metastasis, or otherwise improving overall clinical condition, without necessarily eradicating the cancer.

The composition can also be administered in therapeutically effective amounts as a portion of an anti-cancer cocktail. An anti-cancer cocktail is a mixture of the polypeptide or

modulator of the invention with one or more anti-cancer drugs in addition to a pharmaceutically acceptable carrier for delivery. The use of anti-cancer cocktails as a cancer treatment is routine. Anti-cancer drugs that are well known in the art and can be used as a treatment in combination with the polypeptide or modulator of the invention include: Actinomycin D, Aminoglutethimide, Asparaginase, Bleomycin, Busulfan, Carboplatin, Carmustine, Chlorambucil, Cisplatin (cis-DDP), Cyclophosphamide, Cytarabine HCl (Cytosine arabinoside), Dacarbazine, Dactinomycin, Daunorubicin HCl, Doxorubicin HCl, Estramustine phosphate sodium, Etoposide (V16-213), Floxuridine, 5-Fluorouracil (5-Fu), Flutamide, Hydroxyurea (hydroxycarbamide), Ifosfamide, Interferon Alpha-2a, Interferon Alpha-2b, Leuprolide acetate (LHRH-releasing factor analog), Lomustine, Mechlorethamine HCl (nitrogen mustard), Melphalan, Mercaptopurine, Mesna, Methotrexate (MTX), Mitomycin, Mitoxantrone HCl, Octreotide, Plicamycin, Procarbazine HCl, Streptozocin, Tamoxifen citrate, Thioguanine, Thiotepa, Vinblastine sulfate, Vincristine sulfate, Amsacrine, Azacitidine, Hexamethylmelamine, Interleukin-2, Mitoguazone, Pentostatin, Semustine, Teniposide, and Vindesine sulfate.

In addition, therapeutic compositions of the invention may be used for prophylactic treatment of cancer. There are hereditary conditions and/or environmental situations (*e.g.* exposure to carcinogens) known in the art that predispose an individual to developing cancers. Under these circumstances, it may be beneficial to treat these individuals with therapeutically effective doses of the polypeptide of the invention to reduce the risk of developing cancers.

In vitro models can be used to determine the effective doses of the polypeptide of the invention as a potential cancer treatment. These *in vitro* models include proliferation assays of cultured tumor cells, growth of cultured tumor cells in soft agar (see Freshney, (1987) Culture of Animal Cells: A Manual of Basic Technique, Wily-Liss, New York, NY Ch 18 and Ch 21), tumor systems in nude mice as described in Giovanella et al., J. Natl. Can. Inst., 52: 921-30 (1974), mobility and invasive potential of tumor cells in Boyden Chamber assays as described in Pilkington et al., Anticancer Res., 17: 4107-9 (1997), and angiogenesis assays such as induction of vascularization of the chick chorioallantoic membrane or induction of vascular endothelial cell migration as described in Ribatta et al., Intl. J. Dev. Biol., 40: 1189-97 (1999) and Li et al., Clin. Exp. Metastasis, 17:423-9 (1999), respectively. Suitable tumor cells lines are available, *e.g.* from American Type Tissue Culture Collection catalogs.

4.10.12 RECEPTOR/LIGAND ACTIVITY

A polypeptide of the present invention may also demonstrate activity as receptor, receptor ligand or inhibitor or agonist of receptor/ligand interactions. A polynucleotide of the invention can encode a polypeptide exhibiting such characteristics. Examples of such receptors

and ligands include, without limitation, cytokine receptors and their ligands, receptor kinases and their ligands, receptor phosphatases and their ligands, receptors involved in cell-cell interactions and their ligands (including without limitation, cellular adhesion molecules (such as selectins, integrins and their ligands) and receptor/ligand pairs involved in antigen presentation, antigen recognition and development of cellular and humoral immune responses. Receptors and ligands are also useful for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction. A protein of the present invention (including, without limitation, fragments of receptors and ligands) may themselves be useful as inhibitors of receptor/ligand interactions.

The activity of a polypeptide of the invention may, among other means, be measured by the following methods:

Suitable assays for receptor-ligand activity include without limitation those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A. M. Kruisbeek, D. H. Margulies, E. M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley- Interscience (Chapter 7.28, Measurement of Cellular Adhesion under static conditions 7.28.1- 7.28.22), Takai et al., Proc. Natl. Acad. Sci. USA 84:6864-6868, 1987; Bierer et al., J. Exp. Med. 168:1145-1156, 1988; Rosenstein et al., J. Exp. Med. 169:149-160 1989; Stoltenborg et al., J. Immunol. Methods 175:59-68, 1994; Stitt et al., Cell 80:661-670, 1995.

By way of example, the polypeptides of the invention may be used as a receptor for a ligand(s) thereby transmitting the biological activity of that ligand(s). Ligands may be identified through binding assays, affinity chromatography, dihybrid screening assays, BIAcore assays, gel overlay assays, or other methods known in the art.

Studies characterizing drugs or proteins as agonist or antagonist or partial agonists or a partial antagonist require the use of other proteins as competing ligands. The polypeptides of the present invention or ligand(s) thereof may be labeled by being coupled to radioisotopes, colorimetric molecules or toxin molecules by conventional methods. ("Guide to Protein Purification" Murray P. Deutscher (ed) Methods in Enzymology Vol. 182 (1990) Academic Press, Inc. San Diego). Examples of radioisotopes include, but are not limited to, tritium and carbon-14. Examples of colorimetric molecules include, but are not limited to, fluorescent molecules such as fluorescamine, or rhodamine or other colorimetric molecules. Examples of toxins include, but are not limited, to ricin.

4.10.13 DRUG SCREENING

This invention is particularly useful for screening chemical compounds by using the novel polypeptides or binding fragments thereof in any of a variety of drug screening techniques.

The polypeptides or fragments employed in such a test may either be free in solution, affixed to a solid support, borne on a cell surface or located intracellularly. One method of drug screening utilizes eukaryotic or prokaryotic host cells which are stably transformed with recombinant nucleic acids expressing the polypeptide or a fragment thereof. Drugs are screened against such transformed cells in competitive binding assays. Such cells, either in viable or fixed form, can be used for standard binding assays. One may measure, for example, the formation of complexes between polypeptides of the invention or fragments and the agent being tested or examine the diminution in complex formation between the novel polypeptides and an appropriate cell line, which are well known in the art.

Sources for test compounds that may be screened for ability to bind to or modulate (*i.e.*, increase or decrease) the activity of polypeptides of the invention include (1) inorganic and organic chemical libraries, (2) natural product libraries, and (3) combinatorial libraries comprised of either random or mimetic peptides, oligonucleotides or organic molecules.

Chemical libraries may be readily synthesized or purchased from a number of commercial sources, and may include structural analogs of known compounds or compounds that are identified as "hits" or "leads" via natural product screening.

The sources of natural product libraries are microorganisms (including bacteria and fungi), animals, plants or other vegetation, or marine organisms, and libraries of mixtures for screening may be created by: (1) fermentation and extraction of broths from soil, plant or marine microorganisms or (2) extraction of the organisms themselves. Natural product libraries include polyketides, non-ribosomal peptides, and (non-naturally occurring) variants thereof. For a review, see *Science 282*:63-68 (1998).

Combinatorial libraries are composed of large numbers of peptides, oligonucleotides or organic compounds and can be readily prepared by traditional automated synthesis methods, PCR, cloning or proprietary synthetic methods. Of particular interest are peptide and oligonucleotide combinatorial libraries. Still other libraries of interest include peptide, protein, peptidomimetic, multiparallel synthetic collection, recombinatorial, and polypeptide libraries. For a review of combinatorial chemistry and libraries created therefrom, see Myers, *Curr. Opin. Biotechnol.* 8:701-707 (1997). For reviews and examples of peptidomimetic libraries, see Al-Obeidi et al., *Mol. Biotechnol*, 9(3):205-23 (1998); Hruby et al., *Curr Opin Chem Biol*, 1(1):114-19 (1997); Dorner et al., *Bioorg Med Chem*, 4(5):709-15 (1996) (alkylated dipeptides).

Identification of modulators through use of the various libraries described herein permits modification of the candidate "hit" (or "lead") to optimize the capacity of the "hit" to bind a polypeptide of the invention. The molecules identified in the binding assay are then tested for antagonist or agonist activity in *in vivo* tissue culture or animal models that are well known in the

art. In brief, the molecules are titrated into a plurality of cell cultures or animals and then tested for either cell/animal death or prolonged survival of the animal/cells.

The binding molecules thus identified may be complexed with toxins, *e.g.*, ricin or cholera, or with other compounds that are toxic to cells such as radioisotopes. The toxin-binding molecule complex is then targeted to a tumor or other cell by the specificity of the binding molecule for a polypeptide of the invention. Alternatively, the binding molecules may be complexed with imaging agents for targeting and imaging purposes.

4.10.14 ASSAY FOR RECEPTOR ACTIVITY

The invention also provides methods to detect specific binding of a polypeptide *e.g.* a ligand or a receptor. The art provides numerous assays particularly useful for identifying previously unknown binding partners for receptor polypeptides of the invention. For example, expression cloning using mammalian or bacterial cells, or dihybrid screening assays can be used to identify polynucleotides encoding binding partners. As another example, affinity chromatography with the appropriate immobilized polypeptide of the invention can be used to isolate polypeptides that recognize and bind polypeptides of the invention. There are a number of different libraries used for the identification of compounds, and in particular small molecules, that modulate (*i.e.,* increase or decrease) biological activity of a polypeptide of the invention. Ligands for receptor polypeptides of the invention can also be identified by adding exogenous ligands, or cocktails of ligands to two cells populations that are genetically identical except for the expression of the receptor of the invention: one cell population expresses the receptor of the invention whereas the other does not. The responses of the two cell populations to the addition of ligands(s) are then compared. Alternatively, an expression library can be co-expressed with the polypeptide of the invention in cells and assayed for an autocrine response to identify potential ligand(s). As still another example, BIAcore assays, gel overlay assays, or other methods known in the art can be used to identify binding partner polypeptides, including, (1) organic and inorganic chemical libraries, (2) natural product libraries, and (3) combinatorial libraries comprised of random peptides, oligonucleotides or organic molecules.

The role of downstream intracellular signaling molecules in the signaling cascade of the polypeptide of the invention can be determined. For example, a chimeric protein in which the cytoplasmic domain of the polypeptide of the invention is fused to the extracellular portion of a protein, whose ligand has been identified, is produced in a host cell. The cell is then incubated with the ligand specific for the extracellular portion of the chimeric protein, thereby activating the chimeric receptor. Known downstream proteins involved in intracellular signaling can then

be assayed for expected modifications *i.e.* phosphorylation. Other methods known to those in the art can also be used to identify signaling molecules involved in receptor activity.

4.10.15 ANTI-INFLAMMATORY ACTIVITY

Compositions of the present invention may also exhibit anti-inflammatory activity. The anti-inflammatory activity may be achieved by providing a stimulus to cells involved in the inflammatory response, by inhibiting or promoting cell-cell interactions (such as, for example, cell adhesion), by inhibiting or promoting chemotaxis of cells involved in the inflammatory process, inhibiting or promoting cell extravasation, or by stimulating or suppressing production of other factors which more directly inhibit or promote an inflammatory response. Compositions with such activities can be used to treat inflammatory conditions including chronic or acute conditions), including without limitation intimation associated with infection (such as septic shock, sepsis or systemic inflammatory response syndrome (SIRS)), ischemia-reperfusion injury, endotoxin lethality, arthritis, complement-mediated hyperacute rejection, nephritis, cytokine or chemokine-induced lung injury, inflammatory bowel disease, Crohn's disease or resulting from over production of cytokines such as TNF or IL-1. Compositions of the invention may also be useful to treat anaphylaxis and hypersensitivity to an antigenic substance or material. Compositions of this invention may be utilized to prevent or treat conditions such as, but not limited to, sepsis, acute pancreatitis, endotoxin shock, cytokine induced shock, rheumatoid arthritis, chronic inflammatory arthritis, pancreatic cell damage from diabetes mellitus type 1, graft versus host disease, inflammatory bowel disease, inflamation associated with pulmonary disease, other autoimmune disease or inflammatory disease, an antiproliferative agent such as for acute or chronic mylegenous leukemia or in the prevention of premature labor secondary to intrauterine infections.

4.10.16 LEUKEMIAS

Leukemias and related disorders may be treated or prevented by administration of a therapeutic that promotes or inhibits function of the polynucleotides and/or polypeptides of the invention. Such leukemias and related disorders include but are not limited to acute leukemia, acute lymphocytic leukemia, acute myelocytic leukemia, myeloblastic, promyelocytic, myelomonocytic, monocytic, erythroleukemia, chronic leukemia, chronic myelocytic (granulocytic) leukemia and chronic lymphocytic leukemia (for a review of such disorders, see Fishman et al., 1985, Medicine, 2d Ed., J.B. Lippincott Co., Philadelphia).

4.10.17 NERVOUS SYSTEM DISORDERS

Nervous system disorders, involving cell types which can be tested for efficacy of intervention with compounds that modulate the activity of the polynucleotides and/or polypeptides of the invention, and which can be treated upon thus observing an indication of therapeutic utility, include but are not limited to nervous system injuries, and diseases or disorders which result in either a disconnection of axons, a diminution or degeneration of neurons, or demyelination. Nervous system lesions which may be treated in a patient (including human and non-human mammalian patients) according to the invention include but are not limited to the following lesions of either the central (including spinal cord, brain) or peripheral nervous systems:

(i) traumatic lesions, including lesions caused by physical injury or associated with surgery, for example, lesions which sever a portion of the nervous system, or compression injuries;

(ii) ischemic lesions, in which a lack of oxygen in a portion of the nervous system results in neuronal injury or death, including cerebral infarction or ischemia, or spinal cord infarction or ischemia;

(iii) infectious lesions, in which a portion of the nervous system is destroyed or injured as a result of infection, for example, by an abscess or associated with infection by human immunodeficiency virus, herpes zoster, or herpes simplex virus or with Lyme disease, tuberculosis, syphilis;

(iv) degenerative lesions, in which a portion of the nervous system is destroyed or injured as a result of a degenerative process including but not limited to degeneration associated with Parkinson's disease, Alzheimer's disease, Huntington's chorea, or amyotrophic lateral sclerosis;

(v) lesions associated with nutritional diseases or disorders, in which a portion of the nervous system is destroyed or injured by a nutritional disorder or disorder of metabolism including but not limited to, vitamin B12 deficiency, folic acid deficiency, Wernicke disease, tobacco-alcohol amblyopia, Marchiafava-Bignami disease (primary degeneration of the corpus callosum), and alcoholic cerebellar degeneration;

(vi) neurological lesions associated with systemic diseases including but not limited to diabetes (diabetic neuropathy, Bell's palsy), systemic lupus erythematosus, carcinoma, or sarcoidosis;

(vii) lesions caused by toxic substances including alcohol, lead, or particular neurotoxins; and

(viii) demyelinated lesions in which a portion of the nervous system is destroyed or injured by a demyelinating disease including but not limited to multiple sclerosis, human

immunodeficiency virus-associated myelopathy, transverse myelopathy or various etiologies, progressive multifocal leukoencephalopathy, and central pontine myelinolysis.

Therapeutics which are useful according to the invention for treatment of a nervous system disorder may be selected by testing for biological activity in promoting the survival or differentiation of neurons. For example, and not by way of limitation, therapeutics which elicit any of the following effects may be useful according to the invention:

(i) increased survival time of neurons in culture;

(ii) increased sprouting of neurons in culture or in vivo;

(iii) increased production of a neuron-associated molecule in culture or *in vivo*, *e.g.*, choline acetyltransferase or acetylcholinesterase with respect to motor neurons; or

(iv) decreased symptoms of neuron dysfunction in vivo.

Such effects may be measured by any method known in the art. In preferred, non-limiting embodiments, increased survival of neurons may be measured by the method set forth in Arakawa et al. (1990, J. Neurosci. 10:3507-3515); increased sprouting of neurons may be detected by methods set forth in Pestronk et al. (1980, Exp. Neurol. 70:65-82) or Brown et al. (1981, Ann. Rev. Neurosci. 4:17-42); increased production of neuron-associated molecules may be measured by bioassay, enzymatic assay, antibody binding, Northern blot assay, *etc.*, depending on the molecule to be measured; and motor neuron dysfunction may be measured by assessing the physical manifestation of motor neuron disorder, *e.g.*, weakness, motor neuron conduction velocity, or functional disability.

In specific embodiments, motor neuron disorders that may be treated according to the invention include but are not limited to disorders such as infarction, infection, exposure to toxin, trauma, surgical damage, degenerative disease or malignancy that may affect motor neurons as well as other components of the nervous system, as well as disorders that selectively affect neurons such as amyotrophic lateral sclerosis, and including but not limited to progressive spinal muscular atrophy, progressive bulbar palsy, primary lateral sclerosis, infantile and juvenile muscular atrophy, progressive bulbar paralysis of childhood (Fazio-Londe syndrome), poliomyelitis and the post polio syndrome, and Hereditary Motorsensory Neuropathy (Charcot-Marie-Tooth Disease).

4.10.18 OTHER ACTIVITIES

A polypeptide of the invention may also exhibit one or more of the following additional activities or effects: inhibiting the growth, infection or function of, or killing, infectious agents, including, without limitation, bacteria, viruses, fungi and other parasites; effecting (suppressing or enhancing) bodily characteristics, including, without limitation, height, weight, hair color, eye

color, skin, fat to lean ratio or other tissue pigmentation, or organ or body part size or shape (such as, for example, breast augmentation or diminution, change in bone form or shape); effecting biorhythms or circadian cycles or rhythms; effecting the fertility of male or female subjects; effecting the metabolism, catabolism, anabolism, processing, utilization, storage or elimination of dietary fat, lipid, protein, carbohydrate, vitamins, minerals, co-factors or other nutritional factors or component(s); effecting behavioral characteristics, including, without limitation, appetite, libido, stress, cognition (including cognitive disorders), depression (including depressive disorders) and violent behaviors; providing analgesic effects or other pain reducing effects; promoting differentiation and growth of embryonic stem cells in lineages other than hematopoietic lineages; hormonal or endocrine activity; in the case of enzymes, correcting deficiencies of the enzyme and treating deficiency-related diseases; treatment of hyperproliferative disorders (such as, for example, psoriasis); immunoglobulin-like activity (such as, for example, the ability to bind antigens or complement); and the ability to act as an antigen in a vaccine composition to raise an immune response against such protein or another material or entity which is cross-reactive with such protein.

4.10.19 IDENTIFICATION OF POLYMORPHISMS

The demonstration of polymorphisms makes possible the identification of such polymorphisms in human subjects and the pharmacogenetic use of this information for diagnosis and treatment. Such polymorphisms may be associated with, *e.g.*, differential predisposition or susceptibility to various disease states (such as disorders involving inflammation or immune response) or a differential response to drug administration, and this genetic information can be used to tailor preventive or therapeutic treatment appropriately. For example, the existence of a polymorphism associated with a predisposition to inflammation or autoimmune disease makes possible the diagnosis of this condition in humans by identifying the presence of the polymorphism.

Polymorphisms can be identified in a variety of ways known in the art which all generally involve obtaining a sample from a patient, analyzing DNA from the sample, optionally involving isolation or amplification of the DNA, and identifying the presence of the polymorphism in the DNA. For example, PCR may be used to amplify an appropriate fragment of genomic DNA which may then be sequenced. Alternatively, the DNA may be subjected to allele-specific oligonucleotide hybridization (in which appropriate oligonucleotides are hybridized to the DNA under conditions permitting detection of a single base mismatch) or to a single nucleotide extension assay (in which an oligonucleotide that hybridizes immediately adjacent to the position of the polymorphism is extended with one or more labeled nucleotides).

In addition, traditional restriction fragment length polymorphism analysis (using restriction enzymes that provide differential digestion of the genomic DNA depending on the presence or absence of the polymorphism) may be performed. Arrays with nucleotide sequences of the present invention can be used to detect polymorphisms. The array can comprise modified nucleotide sequences of the present invention in order to detect the nucleotide sequences of the present invention. In the alternative, any one of the nucleotide sequences of the present invention can be placed on the array to detect changes from those sequences.

Alternatively a polymorphism resulting in a change in the amino acid sequence could also be detected by detecting a corresponding change in amino acid sequence of the protein, *e.g.*, by an antibody specific to the variant sequence.

4.10.20 ARTHRITIS AND INFLAMMATION

The immunosuppressive effects of the compositions of the invention against rheumatoid arthritis are determined in an experimental animal model system. The experimental model system is adjuvant induced arthritis in rats, and the protocol is described by J. Holoshitz, et at., 1983, Science, 219:56, or by B. Waksman et al., 1963, Int. Arch. Allergy Appl. Immunol., 23:129. Induction of the disease can be caused by a single injection, generally intradermally, of a suspension of killed Mycobacterium tuberculosis in complete Freund's adjuvant (CFA). The route of injection can vary, but rats may be injected at the base of the tail with an adjuvant mixture. The polypeptide is administered in phosphate buffered solution (PBS) at a dose of about 1-5 mg/kg. The control consists of administering PBS only.

The procedure for testing the effects of the test compound would consist of intradermally injecting killed Mycobacterium tuberculosis in CFA followed by immediately administering the test compound and subsequent treatment every other day until day 24. At 14, 15, 18, 20, 22, and 24 days after injection of Mycobacterium CFA, an overall arthritis score may be obtained as described by J. Holoskitz above. An analysis of the data would reveal that the test compound would have a dramatic affect on the swelling of the joints as measured by a decrease of the arthritis score.

4.11 THERAPEUTIC METHODS

The compositions (including polypeptide fragments, analogs, variants and antibodies or other binding partners or modulators including antisense polynucleotides) of the invention have numerous applications in a variety of therapeutic methods. Examples of therapeutic applications include, but are not limited to, those exemplified herein.

4.11.1 EXAMPLE

One embodiment of the invention is the administration of an effective amount of the polypeptides or other composition of the invention to individuals affected by a disease or disorder that can be modulated by regulating the peptides of the invention. While the mode of administration is not particularly important, parenteral administration is preferred. An exemplary mode of administration is to deliver an intravenous bolus. The dosage of the polypeptides or other composition of the invention will normally be determined by the prescribing physician. It is to be expected that the dosage will vary according to the age, weight, condition and response of the individual patient. Typically, the amount of polypeptide administered per dose will be in the range of about 0.01μg/kg to 100 mg/kg of body weight, with the preferred dose being about 0.1μg/kg to 10 mg/kg of patient body weight. For parenteral administration, polypeptides of the invention will be formulated in an injectable form combined with a pharmaceutically acceptable parenteral vehicle. Such vehicles are well known in the art and examples include water, saline, Ringer's solution, dextrose solution, and solutions consisting of small amounts of the human serum albumin. The vehicle may contain minor amounts of additives that maintain the isotonicity and stability of the polypeptide or other active ingredient. The preparation of such solutions is within the skill of the art.

4.12 PHARMACEUTICAL FORMULATIONS AND ROUTES OF ADMINISTRATION

A protein or other composition of the present invention (from whatever source derived, including without limitation from recombinant and non-recombinant sources and including antibodies and other binding partners of the polypeptides of the invention) may be administered to a patient in need, by itself, or in pharmaceutical compositions where it is mixed with suitable carriers or excipient(s) at doses to treat or ameliorate a variety of disorders. Such a composition may optionally contain (in addition to protein or other active ingredient and a carrier) diluents, fillers, salts, buffers, stabilizers, solubilizers, and other materials well known in the art. The term "pharmaceutically acceptable" means a non-toxic material that does not interfere with the effectiveness of the biological activity of the active ingredient(s). The characteristics of the carrier will depend on the route of administration. The pharmaceutical composition of the invention may also contain cytokines, lymphokines, or other hematopoietic factors such as M-CSF, GM-CSF, TNF, IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, IL-14, IL-15, IFN, TNF0, TNF1, TNF2, G-CSF, Meg-CSF, thrombopoietin, stem cell factor, and erythropoietin. In further compositions, proteins of the invention may be combined with other agents beneficial to the treatment of the disease or disorder in question. These agents

include various growth factors such as epidermal growth factor (EGF), platelet-derived growth factor (PDGF), transforming growth factors (TGF-α and TGF-β), insulin-like growth factor (IGF), as well as cytokines described herein.

The pharmaceutical composition may further contain other agents which either enhance the activity of the protein or other active ingredient or complement its activity or use in treatment. Such additional factors and/or agents may be included in the pharmaceutical composition to produce a synergistic effect with protein or other active ingredient of the invention, or to minimize side effects. Conversely, protein or other active ingredient of the present invention may be included in formulations of the particular clotting factor, cytokine, lymphokine, other hematopoietic factor, thrombolytic or anti-thrombotic factor, or anti-inflammatory agent to minimize side effects of the clotting factor, cytokine, lymphokine, other hematopoietic factor, thrombolytic or anti-thrombotic factor, or anti-inflammatory agent (such as IL-1Ra, IL-1 Hy1, IL-1 Hy2, anti-TNF, corticosteroids, immunosuppressive agents). A protein of the present invention may be active in multimers (*e.g.*, heterodimers or homodimers) or complexes with itself or other proteins. As a result, pharmaceutical compositions of the invention may comprise a protein of the invention in such multimeric or complexed form.

As an alternative to being included in a pharmaceutical composition of the invention including a first protein, a second protein or a therapeutic agent may be concurrently administered with the first protein (*e.g.*, at the same time, or at differing times provided that therapeutic concentrations of the combination of agents is achieved at the treatment site). Techniques for formulation and administration of the compounds of the instant application may be found in "Remington's Pharmaceutical Sciences," Mack Publishing Co., Easton, PA, latest edition. A therapeutically effective dose further refers to that amount of the compound sufficient to result in amelioration of symptoms, *e.g.*, treatment, healing, prevention or amelioration of the relevant medical condition, or an increase in rate of treatment, healing, prevention or amelioration of such conditions. When applied to an individual active ingredient, administered alone, a therapeutically effective dose refers to that ingredient alone. When applied to a combination, a therapeutically effective dose refers to combined amounts of the active ingredients that result in the therapeutic effect, whether administered in combination, serially or simultaneously.

In practicing the method of treatment or use of the present invention, a therapeutically effective amount of protein or other active ingredient of the present invention is administered to a mammal having a condition to be treated. Protein or other active ingredient of the present invention may be administered in accordance with the method of the invention either alone or in combination with other therapies such as treatments employing cytokines, lymphokines or other

hematopoietic factors. When co- administered with one or more cytokines, lymphokines or other hematopoietic factors, protein or other active ingredient of the present invention may be administered either simultaneously with the cytokine(s), lymphokine(s), other hematopoietic factor(s), thrombolytic or anti-thrombotic factors, or sequentially. If administered sequentially, the attending physician will decide on the appropriate sequence of administering protein or other active ingredient of the present invention in combination with cytokine(s), lymphokine(s), other hematopoietic factor(s), thrombolytic or anti-thrombotic factors.

4.12.1 ROUTES OF ADMINISTRATION

Suitable routes of administration may, for example, include oral, rectal, transmucosal, or intestinal administration; parenteral delivery, including intramuscular, subcutaneous, intramedullary injections, as well as intrathecal, direct intraventricular, intravenous, intraperitoneal, intranasal, or intraocular injections. Administration of protein or other active ingredient of the present invention used in the pharmaceutical composition or to practice the method of the present invention can be carried out in a variety of conventional ways, such as oral ingestion, inhalation, topical application or cutaneous, subcutaneous, intraperitoneal, parenteral or intravenous injection. Intravenous administration to the patient is preferred.

Alternately, one may administer the compound in a local rather than systemic manner, for example, via injection of the compound directly into a arthritic joints or in fibrotic tissue, often in a depot or sustained release formulation. In order to prevent the scarring process frequently occurring as complication of glaucoma surgery, the compounds may be administered topically, for example, as eye drops. Furthermore, one may administer the drug in a targeted drug delivery system, for example, in a liposome coated with a specific antibody, targeting, for example, arthritic or fibrotic tissue. The liposomes will be targeted to and taken up selectively by the afflicted tissue.

The polypeptides of the invention are administered by any route that delivers an effective dosage to the desired site of action. The determination of a suitable route of administration and an effective dosage for a particular indication is within the level of skill in the art. Preferably for wound treatment, one administers the therapeutic compound directly to the site. Suitable dosage ranges for the polypeptides of the invention can be extrapolated from these dosages or from similar studies in appropriate animal models. Dosages can then be adjusted as necessary by the clinician to provide maximal therapeutic benefit.

4.12.2 COMPOSITIONS/FORMULATIONS

Pharmaceutical compositions for use in accordance with the present invention thus may be formulated in a conventional manner using one or more physiologically acceptable carriers comprising excipients and auxiliaries which facilitate processing of the active compounds into preparations which can be used pharmaceutically. These pharmaceutical compositions may be manufactured in a manner that is itself known, *e.g.*, by means of conventional mixing, dissolving, granulating, dragee-making, levigating, emulsifying, encapsulating, entrapping or lyophilizing processes. Proper formulation is dependent upon the route of administration chosen. When a therapeutically effective amount of protein or other active ingredient of the present invention is administered orally, protein or other active ingredient of the present invention will be in the form of a tablet, capsule, powder, solution or elixir. When administered in tablet form, the pharmaceutical composition of the invention may additionally contain a solid carrier such as a gelatin or an adjuvant. The tablet, capsule, and powder contain from about 5 to 95% protein or other active ingredient of the present invention, and preferably from about 25 to 90% protein or other active ingredient of the present invention. When administered in liquid form, a liquid carrier such as water, petroleum, oils of animal or plant origin such as peanut oil, mineral oil, soybean oil, or sesame oil, or synthetic oils may be added. The liquid form of the pharmaceutical composition may further contain physiological saline solution, dextrose or other saccharide solution, or glycols such as ethylene glycol, propylene glycol or polyethylene glycol. When administered in liquid form, the pharmaceutical composition contains from about 0.5 to 90% by weight of protein or other active ingredient of the present invention, and preferably from about 1 to 50% protein or other active ingredient of the present invention.

When a therapeutically effective amount of protein or other active ingredient of the present invention is administered by intravenous, cutaneous or subcutaneous injection, protein or other active ingredient of the present invention will be in the form of a pyrogen-free, parenterally acceptable aqueous solution. The preparation of such parenterally acceptable protein or other active ingredient solutions, having due regard to pH, isotonicity, stability, and the like, is within the skill in the art. A preferred pharmaceutical composition for intravenous, cutaneous, or subcutaneous injection should contain, in addition to protein or other active ingredient of the present invention, an isotonic vehicle such as Sodium Chloride Injection, Ringer's Injection, Dextrose Injection, Dextrose and Sodium Chloride Injection, Lactated Ringer's Injection, or other vehicle as known in the art. The pharmaceutical composition of the present invention may also contain stabilizers, preservatives, buffers, antioxidants, or other additives known to those of skill in the art. For injection, the agents of the invention may be formulated in aqueous solutions, preferably in physiologically compatible buffers such as Hanks's solution, Ringer's solution, or physiological saline buffer. For transmucosal administration, penetrants appropriate

to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art.

For oral administration, the compounds can be formulated readily by combining the active compounds with pharmaceutically acceptable carriers well known in the art. Such carriers enable the compounds of the invention to be formulated as tablets, pills, dragees, capsules, liquids, gels, syrups, slurries, suspensions and the like, for oral ingestion by a patient to be treated. Pharmaceutical preparations for oral use can be obtained from a solid excipient, optionally grinding a resulting mixture, and processing the mixture of granules, after adding suitable auxiliaries, if desired, to obtain tablets or dragee cores. Suitable excipients are, in particular, fillers such as sugars, including lactose, sucrose, mannitol, or sorbitol; cellulose preparations such as, for example, maize starch, wheat starch, rice starch, potato starch, gelatin, gum tragacanth, methyl cellulose, hydroxypropylmethyl-cellulose, sodium carboxymethylcellulose, and/or polyvinylpyrrolidone (PVP). If desired, disintegrating agents may be added, such as the cross-linked polyvinyl pyrrolidone, agar, or alginic acid or a salt thereof such as sodium alginate. Dragee cores are provided with suitable coatings. For this purpose, concentrated sugar solutions may be used, which may optionally contain gum arabic, talc, polyvinyl pyrrolidone, carbopol gel, polyethylene glycol, and/or titanium dioxide, lacquer solutions, and suitable organic solvents or solvent mixtures. Dyestuffs or pigments may be added to the tablets or dragee coatings for identification or to characterize different combinations of active compound doses.

Pharmaceutical preparations which can be used orally include push-fit capsules made of gelatin, as well as soft, sealed capsules made of gelatin and a plasticizer, such as glycerol or sorbitol. The push-fit capsules can contain the active ingredients in admixture with filler such as lactose, binders such as starches, and/or lubricants such as talc or magnesium stearate and, optionally, stabilizers. In soft capsules, the active compounds may be dissolved or suspended in suitable liquids, such as fatty oils, liquid paraffin, or liquid polyethylene glycols. In addition, stabilizers may be added. All formulations for oral administration should be in dosages suitable for such administration. For buccal administration, the compositions may take the form of tablets or lozenges formulated in conventional manner.

For administration by inhalation, the compounds for use according to the present invention are conveniently delivered in the form of an aerosol spray presentation from pressurized packs or a nebuliser, with the use of a suitable propellant, *e.g.*, dichlorodifluoromethane, trichlorofluoromethane, dichlorotetrafluoroethane, carbon dioxide or other suitable gas. In the case of a pressurized aerosol the dosage unit may be determined by providing a valve to deliver a metered amount. Capsules and cartridges of, *e.g.*, gelatin for use

in an inhaler or insufflator may be formulated containing a powder mix of the compound and a suitable powder base such as lactose or starch. The compounds may be formulated for parenteral administration by injection, *e.g.*, by bolus injection or continuous infusion. Formulations for injection may be presented in unit dosage form, *e.g.*, in ampules or in multi-dose containers, with an added preservative. The compositions may take such forms as suspensions, solutions or emulsions in oily or aqueous vehicles, and may contain formulatory agents such as suspending, stabilizing and/or dispersing agents.

Pharmaceutical formulations for parenteral administration include aqueous solutions of the active compounds in water-soluble form. Additionally, suspensions of the active compounds may be prepared as appropriate oily injection suspensions. Suitable lipophilic solvents or vehicles include fatty oils such as sesame oil, or synthetic fatty acid esters, such as ethyl oleate or triglycerides, or liposomes. Aqueous injection suspensions may contain substances which increase the viscosity of the suspension, such as sodium carboxymethyl cellulose, sorbitol, or dextran. Optionally, the suspension may also contain suitable stabilizers or agents which increase the solubility of the compounds to allow for the preparation of highly concentrated solutions. Alternatively, the active ingredient may be in powder form for constitution with a suitable vehicle, *e.g.*, sterile pyrogen-free water, before use.

The compounds may also be formulated in rectal compositions such as suppositories or retention enemas, *e.g.*, containing conventional suppository bases such as cocoa butter or other glycerides. In addition to the formulations described previously, the compounds may also be formulated as a depot preparation. Such long acting formulations may be administered by implantation (for example subcutaneously or intramuscularly) or by intramuscular injection. Thus, for example, the compounds may be formulated with suitable polymeric or hydrophobic materials (for example as an emulsion in an acceptable oil) or ion exchange resins, or as sparingly soluble derivatives, for example, as a sparingly soluble salt.

A pharmaceutical carrier for the hydrophobic compounds of the invention is a co-solvent system comprising benzyl alcohol, a nonpolar surfactant, a water-miscible organic polymer, and an aqueous phase. The co-solvent system may be the VPD co-solvent system. VPD is a solution of 3% w/v benzyl alcohol, 8% w/v of the nonpolar surfactant polysorbate 80, and 65% w/v polyethylene glycol 300, made up to volume in absolute ethanol. The VPD co-solvent system (VPD:5W) consists of VPD diluted 1:1 with a 5% dextrose in water solution. This co-solvent system dissolves hydrophobic compounds well, and itself produces low toxicity upon systemic administration. Naturally, the proportions of a co-solvent system may be varied considerably without destroying its solubility and toxicity characteristics. Furthermore, the identity of the co-solvent components may be varied: for example, other low-toxicity nonpolar surfactants may

be used instead of polysorbate 80; the fraction size of polyethylene glycol may be varied; other biocompatible polymers may replace polyethylene glycol, *e.g.* polyvinyl pyrrolidone; and other sugars or polysaccharides may substitute for dextrose. Alternatively, other delivery systems for hydrophobic pharmaceutical compounds may be employed. Liposomes and emulsions are well known examples of delivery vehicles or carriers for hydrophobic drugs. Certain organic solvents such as dimethylsulfoxide also may be employed, although usually at the cost of greater toxicity. Additionally, the compounds may be delivered using a sustained-release system, such as semipermeable matrices of solid hydrophobic polymers containing the therapeutic agent. Various types of sustained-release materials have been established and are well known by those skilled in the art. Sustained-release capsules may, depending on their chemical nature, release the compounds for a few weeks up to over 100 days. Depending on the chemical nature and the biological stability of the therapeutic reagent, additional strategies for protein or other active ingredient stabilization may be employed.

The pharmaceutical compositions also may comprise suitable solid or gel phase carriers or excipients. Examples of such carriers or excipients include but are not limited to calcium carbonate, calcium phosphate, various sugars, starches, cellulose derivatives, gelatin, and polymers such as polyethylene glycols. Many of the active ingredients of the invention may be provided as salts with pharmaceutically compatible counter ions. Such pharmaceutically acceptable base addition salts are those salts which retain the biological effectiveness and properties of the free acids and which are obtained by reaction with inorganic or organic bases such as sodium hydroxide, magnesium hydroxide, ammonia, trialkylamine, dialkylamine, monoalkylamine, dibasic amino acids, sodium acetate, potassium benzoate, triethanol amine and the like.

The pharmaceutical composition of the invention may be in the form of a complex of the protein(s) or other active ingredient(s) of present invention along with protein or peptide antigens. The protein and/or peptide antigen will deliver a stimulatory signal to both B and T lymphocytes. B-lymphocytes will respond to antigen through their surface immunoglobulin receptor. T lymphocytes will respond to antigen through the T cell receptor (TCR) following presentation of the antigen by MHC proteins. MHC and structurally related proteins including those encoded by class I and class II MHC genes on host cells will serve to present the peptide antigen(s) to T lymphocytes. The antigen components could also be supplied as purified MHC-peptide complexes alone or with co-stimulatory molecules that can directly signal T cells. Alternatively antibodies able to bind surface immunoglobulin and other molecules on B cells as well as antibodies able to bind the TCR and other molecules on T cells can be combined with the pharmaceutical composition of the invention.

The pharmaceutical composition of the invention may be in the form of a liposome in which protein of the present invention is combined, in addition to other pharmaceutically acceptable carriers, with amphipathic agents such as lipids which exist in aggregated form as micelles, insoluble monolayers, liquid crystals, or lamellar layers in aqueous solution. Suitable lipids for liposomal formulation include, without limitation, monoglycerides, diglycerides, sulfatides, lysolecithins, phospholipids, saponin, bile acids, and the like. Preparation of such liposomal formulations is within the level of skill in the art, as disclosed, for example, in U.S. Patent Nos. 4,235,871; 4,501,728; 4,837,028; and 4,737,323, all of which are incorporated herein by reference.

The amount of protein or other active ingredient of the present invention in the pharmaceutical composition of the present invention will depend upon the nature and severity of the condition being treated, and on the nature of prior treatments which the patient has undergone. Ultimately, the attending physician will decide the amount of protein or other active ingredient of the present invention with which to treat each individual patient. Initially, the attending physician will administer low doses of protein or other active ingredient of the present invention and observe the patient's response. Larger doses of protein or other active ingredient of the present invention may be administered until the optimal therapeutic effect is obtained for the patient, and at that point the dosage is not increased further. It is contemplated that the various pharmaceutical compositions used to practice the method of the present invention should contain about 0.01 μg to about 100 mg (preferably about 0.1 μg to about 10 mg, more preferably about 0.1 μg to about 1 mg) of protein or other active ingredient of the present invention per kg body weight. For compositions of the present invention which are useful for bone, cartilage, tendon or ligament regeneration, the therapeutic method includes administering the composition topically, systematically, or locally as an implant or device. When administered, the therapeutic composition for use in this invention is, of course, in a pyrogen-free, physiologically acceptable form. Further, the composition may desirably be encapsulated or injected in a viscous form for delivery to the site of bone, cartilage or tissue damage. Topical administration may be suitable for wound healing and tissue repair. Therapeutically useful agents other than a protein or other active ingredient of the invention which may also optionally be included in the composition as described above, may alternatively or additionally, be administered simultaneously or sequentially with the composition in the methods of the invention. Preferably for bone and/or cartilage formation, the composition would include a matrix capable of delivering the protein-containing or other active ingredient-containing composition to the site of bone and/or cartilage damage, providing a structure for the developing bone and cartilage and optimally

capable of being resorbed into the body. Such matrices may be formed of materials presently in use for other implanted medical applications.

The choice of matrix material is based on biocompatibility, biodegradability, mechanical properties, cosmetic appearance and interface properties. The particular application of the compositions will define the appropriate formulation. Potential matrices for the compositions may be biodegradable and chemically defined calcium sulfate, tricalcium phosphate, hydroxyapatite, polylactic acid, polyglycolic acid and polyanhydrides. Other potential materials are biodegradable and biologically well-defined, such as bone or dermal collagen. Further matrices are comprised of pure proteins or extracellular matrix components. Other potential matrices are nonbiodegradable and chemically defined, such as sintered hydroxyapatite, bioglass, aluminates, or other ceramics. Matrices may be comprised of combinations of any of the above-mentioned types of material, such as polylactic acid and hydroxyapatite or collagen and tricalcium phosphate. The bioceramics may be altered in composition, such as in calcium-aluminate-phosphate and processing to alter pore size, particle size, particle shape, and biodegradability. Presently preferred is a 50:50 (mole weight) copolymer of lactic acid and glycolic acid in the form of porous particles having diameters ranging from 150 to 800 microns. In some applications, it will be useful to utilize a sequestering agent, such as carboxymethyl cellulose or autologous blood clot, to prevent the protein compositions from disassociating from the matrix.

A preferred family of sequestering agents is cellulosic materials such as alkylcelluloses (including hydroxyalkylcelluloses), including methylcellulose, ethylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxypropyl-methylcellulose, and carboxymethylcellulose, the most preferred being cationic salts of carboxymethylcellulose (CMC). Other preferred sequestering agents include hyaluronic acid, sodium alginate, poly(ethylene glycol), polyoxyethylene oxide, carboxyvinyl polymer and poly(vinyl alcohol). The amount of sequestering agent useful herein is 0.5-20 wt %, preferably 1-10 wt % based on total formulation weight, which represents the amount necessary to prevent desorption of the protein from the polymer matrix and to provide appropriate handling of the composition, yet not so much that the progenitor cells are prevented from infiltrating the matrix, thereby providing the protein the opportunity to assist the osteogenic activity of the progenitor cells. In further compositions, proteins or other active ingredients of the invention may be combined with other agents beneficial to the treatment of the bone and/or cartilage defect, wound, or tissue in question. These agents include various growth factors such as epidermal growth factor (EGF), platelet derived growth factor (PDGF), transforming growth factors (TGF-α and TGF-β), and insulin-like growth factor (IGF).

The therapeutic compositions are also presently valuable for veterinary applications. Particularly domestic animals and thoroughbred horses, in addition to humans, are desired patients for such treatment with proteins or other active ingredients of the present invention. The dosage regimen of a protein-containing pharmaceutical composition to be used in tissue regeneration will be determined by the attending physician considering various factors which modify the action of the proteins, *e.g.,* amount of tissue weight desired to be formed, the site of damage, the condition of the damaged tissue, the size of a wound, type of damaged tissue (*e.g.*, bone), the patient's age, sex, and diet, the severity of any infection, time of administration and other clinical factors. The dosage may vary with the type of matrix used in the reconstitution and with inclusion of other proteins in the pharmaceutical composition. For example, the addition of other known growth factors, such as IGF I (insulin like growth factor I), to the final composition, may also effect the dosage. Progress can be monitored by periodic assessment of tissue/bone growth and/or repair, for example, X-rays, histomorphometric determinations and tetracycline labeling.

Polynucleotides of the present invention can also be used for gene therapy. Such polynucleotides can be introduced either in vivo or ex vivo into cells for expression in a mammalian subject. Polynucleotides of the invention may also be administered by other known methods for introduction of nucleic acid into a cell or organism (including, without limitation, in the form of viral vectors or naked DNA). Cells may also be cultured ex vivo in the presence of proteins of the present invention in order to proliferate or to produce a desired effect on or activity in such cells. Treated cells can then be introduced in vivo for therapeutic purposes.

4.12.3 EFFECTIVE DOSAGE

Pharmaceutical compositions suitable for use in the present invention include compositions wherein the active ingredients are contained in an effective amount to achieve its intended purpose. More specifically, a therapeutically effective amount means an amount effective to prevent development of or to alleviate the existing symptoms of the subject being treated. Determination of the effective amount is well within the capability of those skilled in the art, especially in light of the detailed disclosure provided herein. For any compound used in the method of the invention, the therapeutically effective dose can be estimated initially from appropriate in vitro assays. For example, a dose can be formulated in animal models to achieve a circulating concentration range that can be used to more accurately determine useful doses in humans. For example, a dose can be formulated in animal models to achieve a circulating concentration range that includes the IC_{50} as determined in cell culture (*i.e.*, the concentration of

the test compound which achieves a half-maximal inhibition of the protein's biological activity). Such information can be used to more accurately determine useful doses in humans.

A therapeutically effective dose refers to that amount of the compound that results in amelioration of symptoms or a prolongation of survival in a patient. Toxicity and therapeutic efficacy of such compounds can be determined by standard pharmaceutical procedures in cell cultures or experimental animals, *e.g.*, for determining the LD_{50} (the dose lethal to 50% of the population) and the ED_{50} (the dose therapeutically effective in 50% of the population). The dose ratio between toxic and therapeutic effects is the therapeutic index and it can be expressed as the ratio between LD_{50} and ED_{50}. Compounds which exhibit high therapeutic indices are preferred. The data obtained from these cell culture assays and animal studies can be used in formulating a range of dosage for use in human. The dosage of such compounds lies preferably within a range of circulating concentrations that include the ED_{50} with little or no toxicity. The dosage may vary within this range depending upon the dosage form employed and the route of administration utilized. The exact formulation, route of administration and dosage can be chosen by the individual physician in view of the patient's condition. See, *e.g.*, Fingl et al., 1975, in "The Pharmacological Basis of Therapeutics", Ch. 1 p.1. Dosage amount and interval may be adjusted individually to provide plasma levels of the active moiety which are sufficient to maintain the desired effects, or minimal effective concentration (MEC). The MEC will vary for each compound but can be estimated from *in vitro* data. Dosages necessary to achieve the MEC will depend on individual characteristics and route of administration. However, HPLC assays or bioassays can be used to determine plasma concentrations.

Dosage intervals can also be determined using MEC value. Compounds should be administered using a regimen that maintains plasma levels above the MEC for 10-90% of the time, preferably between 30-90% and most preferably between 50-90%. In cases of local administration or selective uptake, the effective local concentration of the drug may not be related to plasma concentration.

An exemplary dosage regimen for polypeptides or other compositions of the invention will be in the range of about 0.01 μg/kg to 100 mg/kg of body weight daily, with the preferred dose being about 0.1 μg/kg to 25 mg/kg of patient body weight daily, varying in adults and children. Dosing may be once daily, or equivalent doses may be delivered at longer or shorter intervals.

The amount of composition administered will, of course, be dependent on the subject being treated, on the subject's age and weight, the severity of the affliction, the manner of administration and the judgment of the prescribing physician.

4.12.4 PACKAGING

The compositions may, if desired, be presented in a pack or dispenser device which may contain one or more unit dosage forms containing the active ingredient. The pack may, for example, comprise metal or plastic foil, such as a blister pack. The pack or dispenser device may be accompanied by instructions for administration. Compositions comprising a compound of the invention formulated in a compatible pharmaceutical carrier may also be prepared, placed in an appropriate container, and labeled for treatment of an indicated condition.

4.13 ANTIBODIES

Also included in the invention are antibodies to proteins, or fragments of proteins of the invention. The term "antibody" as used herein refers to immunoglobulin molecules and immunologically active portions of immunoglobulin (Ig) molecules, *i.e.*, molecules that contain an antigen-binding site that specifically binds (immunoreacts with) an antigen. Such antibodies include, but are not limited to, polyclonal, monoclonal, chimeric, single chain, F_{ab}, $F_{ab'}$ and $F_{(ab')2}$ fragments, and an F_{ab} expression library. In general, an antibody molecule obtained from humans relates to any of the classes IgG, IgM, IgA, IgE and IgD, which differ from one another by the nature of the heavy chain present in the molecule. Certain classes have subclasses as well, such as IgG_1, IgG_2, and others. Furthermore, in humans, the light chain may be a kappa chain or a lambda chain. Reference herein to antibodies includes a reference to all such classes, subclasses and types of human antibody species.

An isolated related protein of the invention may be intended to serve as an antigen, or a portion or fragment thereof, and additionally can be used as an immunogen to generate antibodies that immunospecifically bind the antigen, using standard techniques for polyclonal and monoclonal antibody preparation. The full-length protein can be used or, alternatively, the invention provides antigenic peptide fragments of the antigen for use as immunogens. An antigenic peptide fragment comprises at least 6 amino acid residues of the amino acid sequence of the full length protein, (for example the amino acid sequence shown in SEQ ID NO: 30369), and encompasses an epitope thereof such that an antibody raised against the peptide forms a specific immune complex with the full length protein or with any fragment that contains the epitope. Preferably, the antigenic peptide comprises at least 10 amino acid residues, or at least 15 amino acid residues, or at least 20 amino acid residues, or at least 30 amino acid residues. Preferred epitopes encompassed by the antigenic peptide are regions of the protein that are located on its surface; commonly these are hydrophilic regions.

In certain embodiments of the invention, at least one epitope encompassed by the antigenic peptide is a region on the surface of the protein of the invention that is located on the

surface of the protein, *e.g.*, a hydrophilic region. A hydrophobicity analysis of the human related protein sequence will indicate which regions of a related protein are particularly hydrophilic and, therefore, are likely to encode surface residues useful for targeting antibody production. As a means for targeting antibody production, hydropathy plots showing regions of hydrophilicity and hydrophobicity may be generated by any method well known in the art, including, for example, the Kyte Doolittle or the Hopp Woods methods, either with or without Fourier transformation. See, *e.g.*, Hopp and Woods, 1981, *Proc. Nat. Acad. Sci. USA* 78: 3824-3828; Kyte and Doolittle 1982, *J. Mol. Biol.* 157: 105-142, each of which is incorporated herein by reference in its entirety. Antibodies that are specific for one or more domains within an antigenic protein, or derivatives, fragments, analogs or homologs thereof, are also provided herein.

A protein of the invention, or a derivative, fragment, analog, homolog or ortholog thereof, may be utilized as an immunogen in the generation of antibodies that immunospecifically bind these protein components.

Various procedures known within the art may be used for the production of polyclonal or monoclonal antibodies directed against a protein of the invention, or against derivatives, fragments, analogs homologs or orthologs thereof (see, for example, Antibodies: A Laboratory Manual, Harlow E, and Lane D, 1988, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, incorporated herein by reference). Some of these antibodies are discussed below.

5.13.1 Polyclonal Antibodies

For the production of polyclonal antibodies, various suitable host animals (*e.g.*, rabbit, goat, mouse or other mammal) may be immunized by one or more injections with the native protein, a synthetic variant thereof, or a derivative of the foregoing. An appropriate immunogenic preparation can contain, for example, the naturally occurring immunogenic protein, a chemically synthesized polypeptide representing the immunogenic protein, or a recombinantly expressed immunogenic protein. Furthermore, the protein may be conjugated to a second protein known to be immunogenic in the mammal being immunized. Examples of such immunogenic proteins include but are not limited to keyhole limpet hemocyanin, serum albumin, bovine thyroglobulin, and soybean trypsin inhibitor. The preparation can further include an adjuvant. Various adjuvants used to increase the immunological response include, but are not limited to, Freund's (complete and incomplete), mineral gels (*e.g.*, aluminum hydroxide), surface active substances (*e.g.*, lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, dinitrophenol, etc.), adjuvants usable in humans such as Bacille Calmette-Guerin and Corynebacterium parvum, or similar immunostimulatory agents. Additional examples of

adjuvants which can be employed include MPL-TDM adjuvant (monophosphoryl Lipid A, synthetic trehalose dicorynomycolate).

The polyclonal antibody molecules directed against the immunogenic protein can be isolated from the mammal (*e.g.*, from the blood) and further purified by well known techniques, such as affinity chromatography using protein A or protein G, which provide primarily the IgG fraction of immune serum. Subsequently, or alternatively, the specific antigen which is the target of the immunoglobulin sought, or an epitope thereof, may be immobilized on a column to purify the immune specific antibody by immunoaffinity chromatography. Purification of immunoglobulins is discussed, for example, by D. Wilkinson (The Scientist, published by The Scientist, Inc., Philadelphia PA, Vol. 14, No. 8 (April 17, 2000), pp. 25-28).

5.13.2 Monoclonal Antibodies

The term "monoclonal antibody" (MAb) or "monoclonal antibody composition", as used herein, refers to a population of antibody molecules that contain only one molecular species of antibody molecule consisting of a unique light chain gene product and a unique heavy chain gene product. In particular, the complementarity determining regions (CDRs) of the monoclonal antibody are identical in all the molecules of the population. MAbs thus contain an antigen-binding site capable of immunoreacting with a particular epitope of the antigen characterized by a unique binding affinity for it.

Monoclonal antibodies can be prepared using hybridoma methods, such as those described by Kohler and Milstein, Nature, 256:495 (1975). In a hybridoma method, a mouse, hamster, or other appropriate host animal, is typically immunized with an immunizing agent to elicit lymphocytes that produce or are capable of producing antibodies that will specifically bind to the immunizing agent. Alternatively, the lymphocytes can be immunized in vitro.

The immunizing agent will typically include the protein antigen, a fragment thereof or a fusion protein thereof. Generally, either peripheral blood lymphocytes are used if cells of human origin are desired, or spleen cells or lymph node cells are used if non-human mammalian sources are desired. The lymphocytes are then fused with an immortalized cell line using a suitable fusing agent, such as polyethylene glycol, to form a hybridoma cell (Goding, Monoclonal Antibodies: Principles and Practice, Academic Press, (1986) pp. 59-103). Immortalized cell lines are usually transformed mammalian cells, particularly myeloma cells of rodent, bovine and human origin. Usually, rat or mouse myeloma cell lines are employed. The hybridoma cells can be cultured in a suitable culture medium that preferably contains one or more substances that inhibit the growth or survival of the unfused, immortalized cells. For example, if the parental cells lack the enzyme hypoxanthine guanine phosphoribosyl transferase (HGPRT or HPRT), the

culture medium for the hybridomas typically will include hypoxanthine, aminopterin, and thymidine ("HAT medium"), which substances prevent the growth of HGPRT-deficient cells.

Preferred immortalized cell lines are those that fuse efficiently, support stable high level expression of antibody by the selected antibody-producing cells, and are sensitive to a medium such as HAT medium. More preferred immortalized cell lines are murine myeloma lines, which can be obtained, for instance, from the Salk Institute Cell Distribution Center, San Diego, California and the American Type Culture Collection, Manassas, Virginia. Human myeloma and mouse-human heteromyeloma cell lines also have been described for the production of human monoclonal antibodies (Kozbor, J. Immunol., 133:3001 (1984); Brodeur et al., Monoclonal Antibody Production Techniques and Applications, Marcel Dekker, Inc., New York, (1987) pp. 51-63).

The culture medium in which the hybridoma cells are cultured can then be assayed for the presence of monoclonal antibodies directed against the antigen. Preferably, the binding specificity of monoclonal antibodies produced by the hybridoma cells is determined by immunoprecipitation or by an in vitro binding assay, such as radioimmunoassay (RIA) or enzyme-linked immunoabsorbent assay (ELISA). Such techniques and assays are known in the art. The binding affinity of the monoclonal antibody can, for example, be determined by the Scatchard analysis of Munson and Pollard, Anal. Biochem., 107:220 (1980). Preferably, antibodies having a high degree of specificity and a high binding affinity for the target antigen are isolated.

After the desired hybridoma cells are identified, the clones can be subcloned by limiting dilution procedures and grown by standard methods. Suitable culture media for this purpose include, for example, Dulbecco's Modified Eagle's Medium and RPMI-1640 medium. Alternatively, the hybridoma cells can be grown in vivo as ascites in a mammal.

The monoclonal antibodies secreted by the subclones can be isolated or purified from the culture medium or ascites fluid by conventional immunoglobulin purification procedures such as, for example, protein A-Sepharose, hydroxylapatite chromatography, gel electrophoresis, dialysis, or affinity chromatography.

The monoclonal antibodies can also be made by recombinant DNA methods, such as those described in U.S. Patent No. 4,816,567. DNA encoding the monoclonal antibodies of the invention can be readily isolated and sequenced using conventional procedures (*e.g.*, by using oligonucleotide probes that are capable of binding specifically to genes encoding the heavy and light chains of murine antibodies). The hybridoma cells of the invention serve as a preferred source of such DNA. Once isolated, the DNA can be placed into expression vectors, which are then transfected into host cells such as simian COS cells, Chinese hamster ovary (CHO) cells, or

myeloma cells that do not otherwise produce immunoglobulin protein, to obtain the synthesis of monoclonal antibodies in the recombinant host cells. The DNA also can be modified, for example, by substituting the coding sequence for human heavy and light chain constant domains in place of the homologous murine sequences (U.S. Patent No. 4,816,567; Morrison, Nature 368, 812-13 (1994)) or by covalently joining to the immunoglobulin coding sequence all or part of the coding sequence for a non-immunoglobulin polypeptide. Such a non-immunoglobulin polypeptide can be substituted for the constant domains of an antibody of the invention, or can be substituted for the variable domains of one antigen-combining site of an antibody of the invention to create a chimeric bivalent antibody.

5.13.2 Humanized Antibodies

The antibodies directed against the protein antigens of the invention can further comprise humanized antibodies or human antibodies. These antibodies are suitable for administration to humans without engendering an immune response by the human against the administered immunoglobulin. Humanized forms of antibodies are chimeric immunoglobulins, immunoglobulin chains or fragments thereof (such as Fv, Fab, Fab', $F(ab')_2$ or other antigen-binding subsequences of antibodies) that are principally comprised of the sequence of a human immunoglobulin, and contain minimal sequence derived from a non-human immunoglobulin. Humanization can be performed following the method of Winter and co-workers (Jones et al., Nature, 321:522-525 (1986); Riechmann et al., Nature, 332:323-327 (1988); Verhoeyen et al., Science, 239:1534-1536 (1988)), by substituting rodent CDRs or CDR sequences for the corresponding sequences of a human antibody. (See also U.S. Patent No. 5,225,539.) In some instances, Fv framework residues of the human immunoglobulin are replaced by corresponding non-human residues. Humanized antibodies can also comprise residues which are found neither in the recipient antibody nor in the imported CDR or framework sequences. In general, the humanized antibody will comprise substantially all of at least one, and typically two, variable domains, in which all or substantially all of the CDR regions correspond to those of a non-human immunoglobulin and all or substantially all of the framework regions are those of a human immunoglobulin consensus sequence. The humanized antibody optimally also will comprise at least a portion of an immunoglobulin constant region (Fc), typically that of a human immunoglobulin (Jones et al., 1986; Riechmann et al., 1988; and Presta, Curr. Op. Struct. Biol., 2:593-596 (1992)).

5.13.3 Human Antibodies

Fully human antibodies relate to antibody molecules in which essentially the entire sequences of both the light chain and the heavy chain, including the CDRs, arise from human genes. Such antibodies are termed "human antibodies", or "fully human antibodies" herein. Human monoclonal antibodies can be prepared by the trioma technique; the human B-cell hybridoma technique (see Kozbor, et al., 1983 Immunol Today 4: 72) and the EBV hybridoma technique to produce human monoclonal antibodies (see Cole, et al., 1985 In: MONOCLONAL ANTIBODIES AND CANCER THERAPY, Alan R. Liss, Inc., pp. 77-96). Human monoclonal antibodies may be utilized in the practice of the present invention and may be produced by using human hybridomas (see Cote, et al., 1983. Proc Natl Acad Sci USA 80: 2026-2030) or by transforming human B-cells with Epstein Barr Virus in vitro (see Cole, et al., 1985 In: MONOCLONAL ANTIBODIES AND CANCER THERAPY, Alan R. Liss, Inc., pp. 77-96).

In addition, human antibodies can also be produced using additional techniques, including phage display libraries (Hoogenboom and Winter, J. Mol. Biol., 227:381 (1991); Marks et al., J. Mol. Biol., 222:581 (1991)). Similarly, human antibodies can be made by introducing human immunoglobulin loci into transgenic animals, *e.g.*, mice in which the endogenous immunoglobulin genes have been partially or completely inactivated. Upon challenge, human antibody production is observed, which closely resembles that seen in humans in all respects, including gene rearrangement, assembly, and antibody repertoire. This approach is described, for example, in U.S. Patent Nos. 5,545,807; 5,545,806; 5,569,825; 5,625,126; 5,633,425; 5,661,016, and in Marks et al. (Bio/Technology 10, 779-783 (1992)); Lonberg et al. (Nature 368 856-859 (1994)); Morrison (Nature 368, 812-13 (1994)); Fishwild et al,(Nature Biotechnology 14, 845-51 (1996)); Neuberger (Nature Biotechnology 14, 826 (1996)); and Lonberg and Huszar (Intern. Rev. Immunol. 13 65-93 (1995)).

Human antibodies may additionally be produced using transgenic nonhuman animals which are modified so as to produce fully human antibodies rather than the animal's endogenous antibodies in response to challenge by an antigen. (See PCT publication WO94/02602). The endogenous genes encoding the heavy and light immunoglobulin chains in the nonhuman host have been incapacitated, and active loci encoding human heavy and light chain immunoglobulins are inserted into the host's genome. The human genes are incorporated, for example, using yeast artificial chromosomes containing the requisite human DNA segments. An animal which provides all the desired modifications is then obtained as progeny by crossbreeding intermediate transgenic animals containing fewer than the full complement of the modifications. The preferred embodiment of such a nonhuman animal is a mouse, and is termed the Xenomouse™ as disclosed in PCT publications WO 96/33735 and WO 96/34096. This animal produces B cells which secrete fully human immunoglobulins. The antibodies can be obtained directly from

the animal after immunization with an immunogen of interest, as, for example, a preparation of a polyclonal antibody, or alternatively from immortalized B cells derived from the animal, such as hybridomas producing monoclonal antibodies. Additionally, the genes encoding the immunoglobulins with human variable regions can be recovered and expressed to obtain the antibodies directly, or can be further modified to obtain analogs of antibodies such as, for example, single chain Fv molecules.

An example of a method of producing a nonhuman host, exemplified as a mouse, lacking expression of an endogenous immunoglobulin heavy chain is disclosed in U.S. Patent No. 5,939,598. It can be obtained by a method including deleting the J segment genes from at least one endogenous heavy chain locus in an embryonic stem cell to prevent rearrangement of the locus and to prevent formation of a transcript of a rearranged immunoglobulin heavy chain locus, the deletion being effected by a targeting vector containing a gene encoding a selectable marker; and producing from the embryonic stem cell a transgenic mouse whose somatic and germ cells contain the gene encoding the selectable marker.

A method for producing an antibody of interest, such as a human antibody, is disclosed in U.S. Patent No. 5,916,771. It includes introducing an expression vector that contains a nucleotide sequence encoding a heavy chain into one mammalian host cell in culture, introducing an expression vector containing a nucleotide sequence encoding a light chain into another mammalian host cell, and fusing the two cells to form a hybrid cell. The hybrid cell expresses an antibody containing the heavy chain and the light chain.

In a further improvement on this procedure, a method for identifying a clinically relevant epitope on an immunogen, and a correlative method for selecting an antibody that binds immunospecifically to the relevant epitope with high affinity, are disclosed in PCT publication WO 99/53049.

5.13.4 F_{ab} Fragments and Single Chain Antibodies

According to the invention, techniques can be adapted for the production of single-chain antibodies specific to an antigenic protein of the invention (see *e.g.*, U.S. Patent No. 4,946,778). In addition, methods can be adapted for the construction of F_{ab} expression libraries (see *e.g.*, Huse, et al., 1989 Science 246: 1275-1281) to allow rapid and effective identification of monoclonal F_{ab} fragments with the desired specificity for a protein or derivatives, fragments, analogs or homologs thereof. Antibody fragments that contain the idiotypes to a protein antigen may be produced by techniques known in the art including, but not limited to: (i) an $F_{(ab')2}$ fragment produced by pepsin digestion of an antibody molecule; (ii) an F_{ab} fragment generated

by reducing the disulfide bridges of an $F_{(ab')2}$ fragment; (iii) an F_{ab} fragment generated by the treatment of the antibody molecule with papain and a reducing agent and (iv) F_v fragments.

5.13.5 Bispecific Antibodies

Bispecific antibodies are monoclonal, preferably human or humanized, antibodies that have binding specificities for at least two different antigens. In the present case, one of the binding specificities is for an antigenic protein of the invention. The second binding target is any other antigen, and advantageously is a cell-surface protein or receptor or receptor subunit.

Methods for making bispecific antibodies are known in the art. Traditionally, the recombinant production of bispecific antibodies is based on the co-expression of two immunoglobulin heavy-chain/light-chain pairs, where the two heavy chains have different specificities (Milstein and Cuello, Nature, 305:537-539 (1983)). Because of the random assortment of immunoglobulin heavy and light chains, these hybridomas (quadromas) produce a potential mixture of ten different antibody molecules, of which only one has the correct bispecific structure. The purification of the correct molecule is usually accomplished by affinity chromatography steps. Similar procedures are disclosed in WO 93/08829, published 13 May 1993, and in Traunecker *et al.*, 1991 *EMBO J.*, 10:3655-3659.

Antibody variable domains with the desired binding specificities (antibody-antigen combining sites) can be fused to immunoglobulin constant domain sequences. The fusion preferably is with an immunoglobulin heavy-chain constant domain, comprising at least part of the hinge, CH2, and CH3 regions. It is preferred to have the first heavy-chain constant region (CH1) containing the site necessary for light-chain binding present in at least one of the fusions. DNAs encoding the immunoglobulin heavy-chain fusions and, if desired, the immunoglobulin light chain, are inserted into separate expression vectors, and are co-transfected into a suitable host organism. For further details of generating bispecific antibodies see, for example, Suresh et al., Methods in Enzymology, 121:210 (1986).

According to another approach described in WO 96/27011, the interface between a pair of antibody molecules can be engineered to maximize the percentage of heterodimers which are recovered from recombinant cell culture. The preferred interface comprises at least a part of the CH3 region of an antibody constant domain. In this method, one or more small amino acid side chains from the interface of the first antibody molecule are replaced with larger side chains (*e.g.* tyrosine or tryptophan). Compensatory "cavities" of identical or similar size to the large side chain(s) are created on the interface of the second antibody molecule by replacing large amino acid side chains with smaller ones (*e.g.* alanine or threonine). This provides a mechanism for increasing the yield of the heterodimer over other unwanted end-products such as homodimers.

Bispecific antibodies can be prepared as full length antibodies or antibody fragments (*e.g.* $F(ab')_2$ bispecific antibodies). Techniques for generating bispecific antibodies from antibody fragments have been described in the literature. For example, bispecific antibodies can be prepared using chemical linkage. Brennan et al., Science 229:81 (1985) describe a procedure wherein intact antibodies are proteolytically cleaved to generate $F(ab')_2$ fragments. These fragments are reduced in the presence of the dithiol complexing agent sodium arsenite to stabilize vicinal dithiols and prevent intermolecular disulfide formation. The Fab' fragments generated are then converted to thionitrobenzoate (TNB) derivatives. One of the Fab'-TNB derivatives is then reconverted to the Fab'-thiol by reduction with mercaptoethylamine and is mixed with an equimolar amount of the other Fab'-TNB derivative to form the bispecific antibody. The bispecific antibodies produced can be used as agents for the selective immobilization of enzymes.

Additionally, Fab' fragments can be directly recovered from E. coli and chemically coupled to form bispecific antibodies. Shalaby et al., J. Exp. Med. 175:217-225 (1992) describe the production of a fully humanized bispecific antibody $F(ab')_2$ molecule. Each Fab' fragment was separately secreted from E. coli and subjected to directed chemical coupling in vitro to form the bispecific antibody. The bispecific antibody thus formed was able to bind to cells overexpressing the ErbB2 receptor and normal human T cells, as well as trigger the lytic activity of human cytotoxic lymphocytes against human breast tumor targets.

Various techniques for making and isolating bispecific antibody fragments directly from recombinant cell culture have also been described. For example, bispecific antibodies have been produced using leucine zippers. Kostelny et al., J. Immunol. 148(5):1547-1553 (1992). The leucine zipper peptides from the Fos and Jun proteins were linked to the Fab' portions of two different antibodies by gene fusion. The antibody homodimers were reduced at the hinge region to form monomers and then re-oxidized to form the antibody heterodimers. This method can also be utilized for the production of antibody homodimers. The "diabody" technology described by Hollinger et al., Proc. Natl. Acad. Sci. USA 90:6444-6448 (1993) has provided an alternative mechanism for making bispecific antibody fragments. The fragments comprise a heavy-chain variable domain (V_H) connected to a light-chain variable domain (V_L) by a linker which is too short to allow pairing between the two domains on the same chain. Accordingly, the V_H and V_L domains of one fragment are forced to pair with the complementary V_L and V_H domains of another fragment, thereby forming two antigen-binding sites. Another strategy for making bispecific antibody fragments by the use of single-chain Fv (sFv) dimers has also been reported. See, Gruber et al., J. Immunol. 152:5368 (1994).

Antibodies with more than two valencies are contemplated. For example, trispecific antibodies can be prepared. Tutt et al., J. Immunol. 147:60 (1991). Exemplary bispecific antibodies can bind to two different epitopes, at least one of which originates in the protein antigen of the invention. Alternatively, an anti-antigenic arm of an immunoglobulin molecule can be combined with an arm which binds to a triggering molecule on a leukocyte such as a T-cell receptor molecule (*e.g.* CD2, CD3, CD28, or B7), or Fc receptors for IgG (FcγR), such as FcγRI (CD64), FcγRII (CD32) and FcγRIII (CD16) so as to focus cellular defense mechanisms to the cell expressing the particular antigen. Bispecific antibodies can also be used to direct cytotoxic agents to cells which express a particular antigen. These antibodies possess an antigen-binding arm and an arm which binds a cytotoxic agent or a radionuclide chelator, such as EOTUBE, DPTA, DOTA, or TETA. Another bispecific antibody of interest binds the protein antigen described herein and further binds tissue factor (TF).

5.13.6 Heteroconjugate Antibodies

Heteroconjugate antibodies are also within the scope of the present invention. Heteroconjugate antibodies are composed of two covalently joined antibodies. Such antibodies have, for example, been proposed to target immune system cells to unwanted cells (U.S. Patent No. 4,676,980), and for treatment of HIV infection (WO 91/00360; WO 92/200373; EP 03089). It is contemplated that the antibodies can be prepared in vitro using known methods in synthetic protein chemistry, including those involving crosslinking agents. For example, immunotoxins can be constructed using a disulfide exchange reaction or by forming a thioether bond. Examples of suitable reagents for this purpose include iminothiolate and methyl-4-mercaptobutyrimidate and those disclosed, for example, in U.S. Patent No. 4,676,980.

5.13.7 Effector Function Engineering

It can be desirable to modify the antibody of the invention with respect to effector function, so as to enhance, *e.g.*, the effectiveness of the antibody in treating cancer. For example, cysteine residue(s) can be introduced into the Fc region, thereby allowing interchain disulfide bond formation in this region. The homodimeric antibody thus generated can have improved internalization capability and/or increased complement-mediated cell killing and antibody-dependent cellular cytotoxicity (ADCC). See Caron et al., J. Exp Med., 176: 1191-1195 (1992) and Shopes, J. Immunol., 148: 2918-2922 (1992). Homodimeric antibodies with enhanced anti-tumor activity can also be prepared using heterobifunctional cross-linkers as described in Wolff et al. Cancer Research, 53: 2560-2565 (1993). Alternatively, an antibody can

be engineered that has dual Fc regions and can thereby have enhanced complement lysis and ADCC capabilities. See Stevenson et al., Anti-Cancer Drug Design, 3: 219-230 (1989).

5.13.8 Immunoconjugates

The invention also pertains to immunoconjugates comprising an antibody conjugated to a cytotoxic agent such as a chemotherapeutic agent, toxin (*e.g.*, an enzymatically active toxin of bacterial, fungal, plant, or animal origin, or fragments thereof), or a radioactive isotope (*i.e.*, a radioconjugate).

Chemotherapeutic agents useful in the generation of such immunoconjugates have been described above. Enzymatically active toxins and fragments thereof that can be used include diphtheria A chain, nonbinding active fragments of diphtheria toxin, exotoxin A chain (from Pseudomonas aeruginosa), ricin A chain, abrin A chain, modeccin A chain, alpha-sarcin, Aleurites fordii proteins, dianthin proteins, Phytolaca americana proteins (PAPI, PAPII, and PAP-S), momordica charantia inhibitor, curcin, crotin, sapaonaria officinalis inhibitor, gelonin, mitogellin, restrictocin, phenomycin, enomycin, and the tricothecenes. A variety of radionuclides are available for the production of radioconjugated antibodies. Examples include ^{212}Bi, ^{131}I, ^{131}In, ^{90}Y, and ^{186}Re.

Conjugates of the antibody and cytotoxic agent are made using a variety of bifunctional protein-coupling agents such as N-succinimidyl-3-(2-pyridyldithiol) propionate (SPDP), iminothiolane (IT), bifunctional derivatives of imidoesters (such as dimethyl adipimidate HCL), active esters (such as disuccinimidyl suberate), aldehydes (such as glutareldehyde), bis-azido compounds (such as bis (p-azidobenzoyl) hexanediamine), bis-diazonium derivatives (such as bis-(p-diazoniumbenzoyl)-ethylenediamine), diisocyanates (such as tolyene 2,6-diisocyanate), and bis-active fluorine compounds (such as 1,5-difluoro-2,4-dinitrobenzene). For example, a ricin immunotoxin can be prepared as described in Vitetta et al., Science, 238: 1098 (1987). Carbon-14-labeled 1-isothiocyanatobenzyl-3-methyldiethylene triaminepentaacetic acid (MX-DTPA) is an exemplary chelating agent for conjugation of radionucleotide to the antibody. See WO94/11026.

In another embodiment, the antibody can be conjugated to a "receptor" (such streptavidin) for utilization in tumor pretargeting wherein the antibody-receptor conjugate is administered to the patient, followed by removal of unbound conjugate from the circulation using a clearing agent and then administration of a "ligand" (*e.g.*, avidin) that is in turn conjugated to a cytotoxic agent.

4.14 COMPUTER READABLE SEQUENCES

In one application of this embodiment, a nucleotide sequence of the present invention can be recorded on computer readable media. As used herein, "computer readable media" refers to any medium which can be read and accessed directly by a computer. Such media include, but are not limited to: magnetic storage media, such as floppy discs, hard disc storage medium, and magnetic tape; optical storage media such as CD-ROM; electrical storage media such as RAM and ROM; and hybrids of these categories such as magnetic/optical storage media. A skilled artisan can readily appreciate how any of the presently known computer readable mediums can be used to create a manufacture comprising computer readable medium having recorded thereon a nucleotide sequence of the present invention. As used herein, "recorded" refers to a process for storing information on computer readable medium. A skilled artisan can readily adopt any of the presently known methods for recording information on computer readable medium to generate manufactures comprising the nucleotide sequence information of the present invention.

A variety of data storage structures are available to a skilled artisan for creating a computer readable medium having recorded thereon a nucleotide sequence of the present invention. The choice of the data storage structure will generally be based on the means chosen to access the stored information. In addition, a variety of data processor programs and formats can be used to store the nucleotide sequence information of the present invention on computer readable medium. The sequence information can be represented in a word processing text file, formatted in commercially-available software such as WordPerfect and Microsoft Word, or represented in the form of an ASCII file, stored in a database application, such as DB2, Sybase, Oracle, or the like. A skilled artisan can readily adapt any number of data processor structuring formats (*e.g.* text file or database) in order to obtain computer readable medium having recorded thereon the nucleotide sequence information of the present invention.

By providing any of the nucleotide sequences SEQ ID NO: 1-30368 or a representative fragment thereof; or a nucleotide sequence at least 95% identical to any of the nucleotide sequences of SEQ ID NO: 1-30368 in computer readable form, a skilled artisan can routinely access the sequence information for a variety of purposes. Computer software is publicly available which allows a skilled artisan to access sequence information provided in a computer readable medium. The examples which follow demonstrate how software which implements the BLAST (Altschul et al., J. Mol. Biol. 215:403-410 (1990)) and BLAZE (Brutlag et al., Comp. Chem. 17:203-207 (1993)) search algorithms on a Sybase system is used to identify open reading frames (ORFs) within a nucleic acid sequence. Such ORFs may be protein encoding fragments and may be useful in producing commercially important proteins such as enzymes used in fermentation reactions and in the production of commercially useful metabolites.

As used herein, "a computer-based system" refers to the hardware means, software means, and data storage means used to analyze the nucleotide sequence information of the present invention. The minimum hardware means of the computer-based systems of the present invention comprises a central processing unit (CPU), input means, output means, and data storage means. A skilled artisan can readily appreciate that any one of the currently available computer-based systems are suitable for use in the present invention. As stated above, the computer-based systems of the present invention comprise a data storage means having stored therein a nucleotide sequence of the present invention and the necessary hardware means and software means for supporting and implementing a search means. As used herein, "data storage means" refers to memory which can store nucleotide sequence information of the present invention, or a memory access means which can access manufactures having recorded thereon the nucleotide sequence information of the present invention.

As used herein, "search means" refers to one or more programs which are implemented on the computer-based system to compare a target sequence or target structural motif with the sequence information stored within the data storage means. Search means are used to identify fragments or regions of a known sequence which match a particular target sequence or target motif. A variety of known algorithms are disclosed publicly and a variety of commercially available software for conducting search means are and can be used in the computer-based systems of the present invention. Examples of such software includes, but is not limited to, Smith-Waterman, MacPattern (EMBL), BLASTN and BLASTA (NPOLYPEPTIDEIA). A skilled artisan can readily recognize that any one of the available algorithms or implementing software packages for conducting homology searches can be adapted for use in the present computer-based systems. As used herein, a "target sequence" can be any nucleic acid or amino acid sequence of six or more nucleotides or two or more amino acids. A skilled artisan can readily recognize that the longer a target sequence is, the less likely a target sequence will be present as a random occurrence in the database. The most preferred sequence length of a target sequence is from about 10 to 300 amino acids, more preferably from about 30 to 100 nucleotide residues. However, it is well recognized that searches for commercially important fragments, such as sequence fragments involved in gene expression and protein processing, may be of shorter length.

As used herein, "a target structural motif," or "target motif," refers to any rationally selected sequence or combination of sequences in which the sequence(s) are chosen based on a three-dimensional configuration which is formed upon the folding of the target motif. There are a variety of target motifs known in the art. Protein target motifs include, but are not limited to, enzyme active sites and signal sequences. Nucleic acid target motifs include, but are not limited

to, promoter sequences, hairpin structures and inducible expression elements (protein binding sequences).

4.15 TRIPLE HELIX FORMATION

In addition, the fragments of the present invention, as broadly described, can be used to control gene expression through triple helix formation or antisense DNA or RNA, both of which methods are based on the binding of a polynucleotide sequence to DNA or RNA. Polynucleotides suitable for use in these methods are preferably 20 to 40 bases in length and are designed to be complementary to a region of the gene involved in transcription (triple helix - see Lee et al., Nucl. Acids Res. 6:3073 (1979); Cooney et al., Science 15241:456 (1988); and Dervan et al., Science 251:1360 (1991)) or to the mRNA itself (antisense - Olmno, J. Neurochem. 56:560 (1991); Oligodeoxynucleotides as Antisense Inhibitors of Gene Expression, CRC Press, Boca Raton, FL (1988)). Triple helix-formation optimally results in a shut-off of RNA transcription from DNA, while antisense RNA hybridization blocks translation of an mRNA molecule into polypeptide. Both techniques have been demonstrated to be effective in model systems. Information contained in the sequences of the present invention is necessary for the design of an antisense or triple helix oligonucleotide.

4.16 DIAGNOSTIC ASSAYS AND KITS

The present invention further provides methods to identify the presence or expression of one of the ORFs of the present invention, or homolog thereof, in a test sample, using a nucleic acid probe or antibodies of the present invention, optionally conjugated or otherwise associated with a suitable label.

In general, methods for detecting a polynucleotide of the invention can comprise contacting a sample with a compound that binds to and forms a complex with the polynucleotide for a period sufficient to form the complex, and detecting the complex, so that if a complex is detected, a polynucleotide of the invention is detected in the sample. Such methods can also comprise contacting a sample under stringent hybridization conditions with nucleic acid primers that anneal to a polynucleotide of the invention under such conditions, and amplifying annealed polynucleotides, so that if a polynucleotide is amplified, a polynucleotide of the invention is detected in the sample.

In general, methods for detecting a polypeptide of the invention can comprise contacting a sample with a compound that binds to and forms a complex with the polypeptide for a period sufficient to form the complex, and detecting the complex, so that if a complex is detected, a polypeptide of the invention is detected in the sample.

In detail, such methods comprise incubating a test sample with one or more of the antibodies or one or more of the nucleic acid probes of the present invention and assaying for binding of the nucleic acid probes or antibodies to components within the test sample.

Conditions for incubating a nucleic acid probe or antibody with a test sample vary. Incubation conditions depend on the format employed in the assay, the detection methods employed, and the type and nature of the nucleic acid probe or antibody used in the assay. One skilled in the art will recognize that any one of the commonly available hybridization, amplification or immunological assay formats can readily be adapted to employ the nucleic acid probes or antibodies of the present invention. Examples of such assays can be found in Chard, T., An Introduction to Radioimmunoassay and Related Techniques, Elsevier Science Publishers, Amsterdam, The Netherlands (1986); Bullock, G.R. et al., Techniques in Immunocytochemistry, Academic Press, Orlando, FL Vol. 1 (1982), Vol. 2 (1983), Vol. 3 (1985); Tijssen, P., Practice and Theory of immunoassays: Laboratory Techniques in Biochemistry and Molecular Biology, Elsevier Science Publishers, Amsterdam, The Netherlands (1985). The test samples of the present invention include cells, protein or membrane extracts of cells, or biological fluids such as sputum, blood, serum, plasma, or urine. The test sample used in the above-described method will vary based on the assay format, nature of the detection method and the tissues, cells or extracts used as the sample to be assayed. Methods for preparing protein extracts or membrane extracts of cells are well known in the art and can be readily be adapted in order to obtain a sample which is compatible with the system utilized.

In another embodiment of the present invention, kits are provided which contain the necessary reagents to carry out the assays of the present invention. Specifically, the invention provides a compartment kit to receive, in close confinement, one or more containers which comprises: (a) a first container comprising one of the probes or antibodies of the present invention; and (b) one or more other containers comprising one or more of the following: wash reagents, reagents capable of detecting presence of a bound probe or antibody.

In detail, a compartment kit includes any kit in which reagents are contained in separate containers. Such containers include small glass containers, plastic containers or strips of plastic or paper. Such containers allows one to efficiently transfer reagents from one compartment to another compartment such that the samples and reagents are not cross-contaminated, and the agents or solutions of each container can be added in a quantitative fashion from one compartment to another. Such containers will include a container which will accept the test sample, a container which contains the antibodies used in the assay, containers which contain wash reagents (such as phosphate buffered saline, Tris-buffers, etc.), and containers which contain the reagents used to detect the bound antibody or probe. Types of detection reagents

include labeled nucleic acid probes, labeled secondary antibodies, or in the alternative, if the primary antibody is labeled, the enzymatic, or antibody binding reagents which are capable of reacting with the labeled antibody. One skilled in the art will readily recognize that the disclosed probes and antibodies of the present invention can be readily incorporated into one of the established kit formats which are well known in the art.

4.17 MEDICAL IMAGING

The novel polypeptides and binding partners of the invention are useful in medical imaging of sites expressing the molecules of the invention (*e.g.*, where the polypeptide of the invention is involved in the immune response, for imaging sites of inflammation or infection). See, *e.g.*, Kunkel et al., U.S. Pat. NO. 5,413,778. Such methods involve chemical attachment of a labeling or imaging agent, administration of the labeled polypeptide to a subject in a pharmaceutically acceptable carrier, and imaging the labeled polypeptide *in vivo* at the target site.

4.18 SCREENING ASSAYS

Using the isolated proteins and polynucleotides of the invention, the present invention further provides methods of obtaining and identifying agents which bind to a polypeptide encoded by an ORF corresponding to any of the nucleotide sequences set forth in SEQ ID NO: 1-30368, or bind to a specific domain of the polypeptide encoded by the nucleic acid. In detail, said method comprises the steps of:

(a) contacting an agent with an isolated protein encoded by an ORF of the present invention, or nucleic acid of the invention; and

(b) determining whether the agent binds to said protein or said nucleic acid.

In general, therefore, such methods for identifying compounds that bind to a polynucleotide of the invention can comprise contacting a compound with a polynucleotide of the invention for a time sufficient to form a polynucleotide/compound complex, and detecting the complex, so that if a polynucleotide/compound complex is detected, a compound that binds to a polynucleotide of the invention is identified.

Likewise, in general, therefore, such methods for identifying compounds that bind to a polypeptide of the invention can comprise contacting a compound with a polypeptide of the invention for a time sufficient to form a polypeptide/compound complex, and detecting the complex, so that if a polypeptide/compound complex is detected, a compound that binds to a polynucleotide of the invention is identified.

Methods for identifying compounds that bind to a polypeptide of the invention can also comprise contacting a compound with a polypeptide of the invention in a cell for a time sufficient to form a polypeptide/compound complex, wherein the complex drives expression of a receptor gene sequence in the cell, and detecting the complex by detecting reporter gene sequence expression, so that if a polypeptide/compound complex is detected, a compound that binds a polypeptide of the invention is identified.

Compounds identified via such methods can include compounds which modulate the activity of a polypeptide of the invention (that is, increase or decrease its activity, relative to activity observed in the absence of the compound). Alternatively, compounds identified via such methods can include compounds which modulate the expression of a polynucleotide of the invention (that is, increase or decrease expression relative to expression levels observed in the absence of the compound). Compounds, such as compounds identified via the methods of the invention, can be tested using standard assays well known to those of skill in the art for their ability to modulate activity/expression.

The agents screened in the above assay can be, but are not limited to, peptides, carbohydrates, vitamin derivatives, or other pharmaceutical agents. The agents can be selected and screened at random or rationally selected or designed using protein modeling techniques.

For random screening, agents such as peptides, carbohydrates, pharmaceutical agents and the like are selected at random and are assayed for their ability to bind to the protein encoded by the ORF of the present invention. Alternatively, agents may be rationally selected or designed. As used herein, an agent is said to be "rationally selected or designed" when the agent is chosen based on the configuration of the particular protein. For example, one skilled in the art can readily adapt currently available procedures to generate peptides, pharmaceutical agents and the like, capable of binding to a specific peptide sequence, in order to generate rationally designed antipeptide peptides, for example see Hurby et al., Application of Synthetic Peptides: Antisense Peptides," In Synthetic Peptides, A User's Guide, W.H. Freeman, NY (1992), pp. 289-307, and Kaspczak et al., Biochemistry 28:9230-8 (1989), or pharmaceutical agents, or the like.

In addition to the foregoing, one class of agents of the present invention, as broadly described, can be used to control gene expression through binding to one of the ORFs or EMFs of the present invention. As described above, such agents can be randomly screened or rationally designed/selected. Targeting the ORF or EMF allows a skilled artisan to design sequence specific or element specific agents, modulating the expression of either a single ORF or multiple ORFs which rely on the same EMF for expression control. One class of DNA binding agents are agents which contain base residues which hybridize or form a triple helix formation by binding to DNA or RNA. Such agents can be based on the classic phosphodiester,

ribonucleic acid backbone, or can be a variety of sulfhydryl or polymeric derivatives which have base attachment capacity.

Agents suitable for use in these methods preferably contain 20 to 40 bases and are designed to be complementary to a region of the gene involved in transcription (triple helix - see Lee et al., Nucl. Acids Res. 6:3073 (1979); Cooney et al., Science 241:456 (1988); and Dervan et al., Science 251:1360 (1991)) or to the mRNA itself (antisense - Okano, J. Neurochem. 56:560 (1991); Oligodeoxynucleotides as Antisense Inhibitors of Gene Expression, CRC Press, Boca Raton, FL (1988)). Triple helix-formation optimally results in a shut-off of RNA transcription from DNA, while antisense RNA hybridization blocks translation of an mRNA molecule into polypeptide. Both techniques have been demonstrated to be effective in model systems. Information contained in the sequences of the present invention is necessary for the design of an antisense or triple helix oligonucleotide and other DNA binding agents.

Agents that bind to a protein encoded by one of the ORFs of the present invention can be used as a diagnostic agent. Agents which bind to a protein encoded by one of the ORFs of the present invention can be formulated using known techniques to generate a pharmaceutical composition.

4.19 USE OF NUCLEIC ACIDS AS PROBES

Another aspect of the subject invention is to provide for polypeptide-specific nucleic acid hybridization probes capable of hybridizing with naturally occurring nucleotide sequences. The hybridization probes of the subject invention may be derived from any of the nucleotide sequences SEQ ID NO: 1-30368. Because the corresponding gene is only expressed in a limited number of tissues, a hybridization probe derived from of any of the nucleotide sequences SEQ ID NO: 1-30368 can be used as an indicator of the presence of RNA of cell type of such a tissue in a sample.

Any suitable hybridization technique can be employed, such as, for example, in situ hybridization. PCR as described in US Patents Nos. 4,683,195 and 4,965,188 provides additional uses for oligonucleotides based upon the nucleotide sequences. Such probes used in PCR may be of recombinant origin, may be chemically synthesized, or a mixture of both. The probe will comprise a discrete nucleotide sequence for the detection of identical sequences or a degenerate pool of possible sequences for identification of closely related genomic sequences.

Other means for producing specific hybridization probes for nucleic acids include the cloning of nucleic acid sequences into vectors for the production of mRNA probes. Such vectors are known in the art and are commercially available and may be used to synthesize RNA probes *in vitro* by means of the addition of the appropriate RNA polymerase as T7 or SP6 RNA

polymerase and the appropriate radioactively labeled nucleotides. The nucleotide sequences may be used to construct hybridization probes for mapping their respective genomic sequences. The nucleotide sequence provided herein may be mapped to a chromosome or specific regions of a chromosome using well known genetic and/or chromosomal mapping techniques. These techniques include in situ hybridization, linkage analysis against known chromosomal markers, hybridization screening with libraries or flow-sorted chromosomal preparations specific to known chromosomes, and the like. The technique of fluorescent in situ hybridization of chromosome spreads has been described, among other places, in Verma et al (1988) Human Chromosomes: A Manual of Basic Techniques, Pergamon Press, New York NY.

Fluorescent *in situ* hybridization of chromosomal preparations and other physical chromosome mapping techniques may be correlated with additional genetic map data. Examples of genetic map data can be found in the 1994 Genome Issue of Science (265:1981f). Correlation between the location of a nucleic acid on a physical chromosomal map and a specific disease (or predisposition to a specific disease) may help delimit the region of DNA associated with that genetic disease. The nucleotide sequences of the subject invention may be used to detect differences in gene sequences between normal, carrier or affected individuals.

4.20 PREPARATION OF SUPPORT BOUND OLIGONUCLEOTIDES

Oligonucleotides, *i.e.*, small nucleic acid segments, may be readily prepared by, for example, directly synthesizing the oligonucleotide by chemical means, as is commonly practiced using an automated oligonucleotide synthesizer.

Support bound oligonucleotides may be prepared by any of the methods known to those of skill in the art using any suitable support such as glass, polystyrene or Teflon. One strategy is to precisely spot oligonucleotides synthesized by standard synthesizers. Immobilization can be achieved using passive adsorption (Inouye & Hondo, (1990) J. Clin. Microbiol. 28(6) 1469-72); using UV light (Nagata *et al.*, 1985; Dahlen *et al.*, 1987; Morrissey & Collins, (1989) Mol. Cell Probes 3(2) 189-207) or by covalent binding of base modified DNA (Keller *et al.*, 1988; 1989); all references being specifically incorporated herein.

Another strategy that may be employed is the use of the strong biotin-streptavidin interaction as a linker. For example, Broude *et al.* (1994) Proc. Natl. Acad. Sci. USA 91(8) 3072-6, describe the use of biotinylated probes, although these are duplex probes, that are immobilized on streptavidin-coated magnetic beads. Streptavidin-coated beads may be purchased from Dynal, Oslo. Of course, this same linking chemistry is applicable to coating any surface with streptavidin. Biotinylated probes may be purchased from various sources, such as, *e.g.*, Operon Technologies (Alameda, CA).

Nunc Laboratories (Naperville, IL) is also selling suitable material that could be used. Nunc Laboratories have developed a method by which DNA can be covalently bound to the microwell surface termed Covalink NH. CovaLink NH is a polystyrene surface grafted with secondary amino groups (>NH) that serve as bridge-heads for further covalent coupling. CovaLink Modules may be purchased from Nunc Laboratories. DNA molecules may be bound to CovaLink exclusively at the 5'-end by a phosphoramidate bond, allowing immobilization of more than 1 pmol of DNA (Rasmussen *et al.,* (1991) Anal. Biochem. 198(1) 138-42).

The use of CovaLink NH strips for covalent binding of DNA molecules at the 5'-end has been described (Rasmussen et al., (1991). In this technology, a phosphoramidate bond is employed (Chu et al., (1983) Nucleic Acids Res. 11(8) 6513-29). This is beneficial as immobilization using only a single covalent bond is preferred. The phosphoramidate bond joins the DNA to the CovaLink NH secondary amino groups that are positioned at the end of spacer arms covalently grafted onto the polystyrene surface through a 2 nm long spacer arm. To link an oligonucleotide to CovaLink NH via an phosphoramidate bond, the oligonucleotide terminus must have a 5'-end phosphate group. It is, perhaps, even possible for biotin to be covalently bound to CovaLink and then streptavidin used to bind the probes.

More specifically, the linkage method includes dissolving DNA in water (7.5 ng/ul) and denaturing for 10 min. at 95°C and cooling on ice for 10 min. Ice-cold 0.1 M 1-methylimidazole, pH 7.0 (1-MeIm$_7$), is then added to a final concentration of 10 mM 1-MeIm$_7$. A ss DNA solution is then dispensed into CovaLink NH strips (75 ul/well) standing on ice.

Carbodiimide 0.2 M 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide (EDC), dissolved in 10 mM 1-MeIm$_7$, is made fresh and 25 ul added per well. The strips are incubated for 5 hours at 50°C. After incubation the strips are washed using, *e.g.*, Nunc-Immuno Wash; first the wells are washed 3 times, then they are soaked with washing solution for 5 min., and finally they are washed 3 times (where in the washing solution is 0.4 N NaOH, 0.25% SDS heated to 50°C).

It is contemplated that a further suitable method for use with the present invention is that described in PCT Patent Application WO 90/03382 (Southern & Maskos), incorporated herein by reference. This method of preparing an oligonucleotide bound to a support involves attaching a nucleoside 3'-reagent through the phosphate group by a covalent phosphodiester link to aliphatic hydroxyl groups carried by the support. The oligonucleotide is then synthesized on the supported nucleoside and protecting groups removed from the synthetic oligonucleotide chain under standard conditions that do not cleave the oligonucleotide from the support. Suitable reagents include nucleoside phosphoramidite and nucleoside hydrogen phosphorate.

An on-chip strategy for the preparation of DNA probe for the preparation of DNA probe arrays may be employed. For example, addressable laser-activated photodeprotection may be

employed in the chemical synthesis of oligonucleotides directly on a glass surface, as described by Fodor *et al.* (1991) Science 251(4995) 767-73, incorporated herein by reference. Probes may also be immobilized on nylon supports as described by Van Ness *et al.* (1991) Nucleic Acids Res. 19(12) 3345-50; or linked to Teflon using the method of Duncan & Cavalier (1988) Anal. Biochem. 169(1) 104-8; all references being specifically incorporated herein.

To link an oligonucleotide to a nylon support, as described by Van Ness *et al.* (1991), requires activation of the nylon surface via alkylation and selective activation of the 5'-amine of oligonucleotides with cyanuric chloride.

One particular way to prepare support bound oligonucleotides is to utilize the light-generated synthesis described by Pease *et al.*, (1994) PNAS USA 91(11) 5022-6, incorporated herein by reference). These authors used current photolithographic techniques to generate arrays of immobilized oligonucleotide probes (DNA chips). These methods, in which light is used to direct the synthesis of oligonucleotide probes in high-density, miniaturized arrays, utilize photolabile 5'-protected *N*-acyl-deoxynucleoside phosphoramidites, surface linker chemistry and versatile combinatorial synthesis strategies. A matrix of 256 spatially defined oligonucleotide probes may be generated in this manner.

4.21 PREPARATION OF NUCLEIC ACID FRAGMENTS

The nucleic acids may be obtained from any appropriate source, such as cDNAs, genomic DNA, chromosomal DNA, microdissected chromosome bands, cosmid or YAC inserts, and RNA, including mRNA without any amplification steps. For example, Sambrook *et al.* (1989) describes three protocols for the isolation of high molecular weight DNA from mammalian cells (p. 9.14-9.23).

DNA fragments may be prepared as clones in M13, plasmid or lambda vectors and/or prepared directly from genomic DNA or cDNA by PCR or other amplification methods. Samples may be prepared or dispensed in multiwell plates. About 100-1000 ng of DNA samples may be prepared in 2-500 ml of final volume.

The nucleic acids would then be fragmented by any of the methods known to those of skill in the art including, for example, using restriction enzymes as described at 9.24-9.28 of Sambrook *et al.* (1989), shearing by ultrasound and NaOH treatment.

Low pressure shearing is also appropriate, as described by Schriefer *et al.* (1990) Nucleic Acids Res. 18(24) 7455-6, incorporated herein by reference). In this method, DNA samples are passed through a small French pressure cell at a variety of low to intermediate pressures. A lever device allows controlled application of low to intermediate pressures to the cell. The results of

these studies indicate that low-pressure shearing is a useful alternative to sonic and enzymatic DNA fragmentation methods.

One particularly suitable way for fragmenting DNA is contemplated to be that using the two base recognition endonuclease, *Cvi*JI, described by Fitzgerald *et al.* (1992) Nucleic Acids Res. 20(14) 3753-62. These authors described an approach for the rapid fragmentation and fractionation of DNA into particular sizes that they contemplated to be suitable for shotgun cloning and sequencing.

The restriction endonuclease *Cvi*JI normally cleaves the recognition sequence PuGCPy between the G and C to leave blunt ends. Atypical reaction conditions, which alter the specificity of this enzyme (*Cvi*JI**), yield a quasi-random distribution of DNA fragments form the small molecule pUC19 (2688 base pairs). Fitzgerald *et al.* (1992) quantitatively evaluated the randomness of this fragmentation strategy, using a *Cvi*JI** digest of pUC19 that was size fractionated by a rapid gel filtration method and directly ligated, without end repair, to a lac Z minus M13 cloning vector. Sequence analysis of 76 clones showed that *Cvi*JI** restricts pyGCPy and PuGCPu, in addition to PuGCPy sites, and that new sequence data is accumulated at a rate consistent with random fragmentation.

As reported in the literature, advantages of this approach compared to sonication and agarose gel fractionation include: smaller amounts of DNA are required (0.2-0.5 ug instead of 2-5 ug); and fewer steps are involved (no preligation, end repair, chemical extraction, or agarose gel electrophoresis and elution are needed.

Irrespective of the manner in which the nucleic acid fragments are obtained or prepared, it is important to denature the DNA to give single stranded pieces available for hybridization. This is achieved by incubating the DNA solution for 2-5 minutes at 80-90°C. The solution is then cooled quickly to 2°C to prevent renaturation of the DNA fragments before they are contacted with the chip. Phosphate groups must also be removed from genomic DNA by methods known in the art.

4.22 PREPARATION OF DNA ARRAYS

Arrays may be prepared by spotting DNA samples on a support such as a nylon membrane. Spotting may be performed by using arrays of metal pins (the positions of which correspond to an array of wells in a microtiter plate) to repeated by transfer of about 20 nl of a DNA solution to a nylon membrane. By offset printing, a density of dots higher than the density of the wells is achieved. One to 25 dots may be accommodated in 1 mm^2, depending on the type of label used. By avoiding spotting in some preselected number of rows and columns, separate subsets (subarrays) may be formed. Samples in one subarray may be the same genomic segment of DNA (or the same gene) from different individuals, or may be different, overlapped genomic clones. Each of the

subarrays may represent replica spotting of the same samples. In one example, a selected gene segment may be amplified from 64 patients. For each patient, the amplified gene segment may be in one 96-well plate (all 96 wells containing the same sample). A plate for each of the 64 patients is prepared. By using a 96-pin device, all samples may be spotted on one 8 x 12 cm membrane. Subarrays may contain 64 samples, one from each patient. Where the 96 subarrays are identical, the dot span may be 1 mm^2 and there may be a 1 mm space between subarrays.

Another approach is to use membranes or plates (available from NUNC, Naperville, Illinois) which may be partitioned by physical spacers *e.g.* a plastic grid molded over the membrane, the grid being similar to the sort of membrane applied to the bottom of multiwell plates, or hydrophobic strips. A fixed physical spacer is not preferred for imaging by exposure to flat phosphor-storage screens or x-ray films.

The present invention is illustrated in the following examples. Upon consideration of the present disclosure, one of skill in the art will appreciate that many other embodiments and variations may be made in the scope of the present invention. Accordingly, it is intended that the broader aspects of the present invention not be limited to the disclosure of the following examples. The present invention is not to be limited in scope by the exemplified embodiments which are intended as illustrations of single aspects of the invention, and compositions and methods which are functionally equivalent are within the scope of the invention. Indeed, numerous modifications and variations in the practice of the invention are expected to occur to those skilled in the art upon consideration of the present preferred embodiments. Consequently, the only limitations which should be placed upon the scope of the invention are those which appear in the appended claims.

All references cited within the body of the instant specification are hereby incorporated by reference in their entirety.

5.0 EXAMPLES

5.1 EXAMPLE 1

Novel Nucleic Acid Sequences Obtained From Various Libraries

A plurality of novel nucleic acids were obtained from cDNA libraries prepared from various human tissues and in some cases isolated from a genomic library derived from human chromosome using standard PCR, SBH sequence signature analysis and Sanger sequencing techniques. The inserts of the library were amplified with PCR using primers specific for the vector sequences which flank the inserts. Clones from cDNA libraries were spotted on nylon membrane filters and screened with oligonucleotide probes (*e.g.*, 7-mers) to obtain signature sequences. The clones were clustered into groups of similar or identical sequences. Representative clones were selected for sequencing.

In some cases, the 5' sequence of the amplified inserts was then deduced using a typical Sanger sequencing protocol. PCR products were purified and subjected to fluorescent dye terminator cycle sequencing. Single pass gel sequencing was done using a 377 Applied Biosystems (ABI) sequencer to obtain the novel nucleic acid sequences. In some cases RACE (Rapid Amplification of cDNA Ends) was performed to further extend the sequence in the 5' direction.

5.2 EXAMPLE 2

Novel Contigs

The novel contigs of the invention were assembled from sequences that were obtained from a cDNA library by methods described in Example 1 above, and in some cases sequences obtained from one or more public databases. The sequences for the resulting nucleic acid contigs are designated as SEQ ID NO: 1-30368 and are provided in the attached Sequence Listing. The contigs were assembled using an EST sequence as a seed. Then a recursive algorithm was used to extend the seed EST into an extended assemblage, by pulling additional sequences from different databases (*i.e.*, Hyseq's database containing EST sequences, dbEST version 115, gb pri 115, and UniGene version 103, and exons from public domain genomic sequences predicted by GenScan) that belong to this assemblage. The algorithm terminated when there was no additional sequences from the above databases that would extend the assemblage. Further, the inclusion of component sequences into the assemblage was based on a BLASTN hit to the extending assemblage with BLAST score greater than 300 and percent identity greater than 95%.

The novel predicted polypeptides (including proteins) encoded by the novel polynucleotides (SEQ ID NO: 1-30368) of the present invention are incorporated in the attached Sequence Listing. A subset the predicted polypeptide sequences contain an unknown amino acid, a stop codon, a possible nucleotide deletion or a possible nucleotide insertion. These sequences have been shown in their entirety with the special characters in Table 2. Table 2 also shows the corresponding start and stop nucleotide locations to each of SEQ ID NO: 1-30368. Table 2 also indicates the method by which the polypeptide was predicted. Method A refers to a polypeptide obtained by using a software program called FASTY (available from http://fasta.bioch.virginia.edu) which selects a polypeptide based on a comparison of the translated novel polynucleotide to known polynucleotides (W.R. Pearson, Methods in Enzymology, 183:63-98 (1990), herein incorporated by reference). Method B refers to a polypeptide obtained by using a software program called GenScan for human/vertebrate sequences (available from Stanford University, Office of Technology Licensing) that predicts the polypeptide based on a probabilistic model of gene structure/compositional properties (C. Burge and S. Karlin, J. Mol. Biol.. 268:78-94 (1997), incorporated herein by

reference). Method C refers to a polypeptide obtained by using a Hyseq proprietary software program that translates the novel polynucleotide and its complementary strand into six possible amino acid sequences (forward and reverse frames) and chooses the polypeptide with the longest open reading frame.

The nearest neighbor results for SEQ ID NO: 1-30368 were obtained by a BLASTP version 2.0al 19MP-WashU search against Genpept release 121 and Geneseq release 200103 (Derwent), using BLAST algorithm. The nearest neighbor result showed the closest homologue for SEQ ID NO: 1-30368. The nearest neighbor results for SEQ ID NO: 1-30368 are incorporated in the attached Sequence Listing.

Using eMatrix software package (Stanford University, Stanford, CA) (Wu et al., J. Comp. Biol., Vol. 6 pp. 219-235 (1999) herein incorporated by reference), all the sequences were examined to determine whether they had identifiable signature regions. The attached Sequence Listing provodes the results obtained by eMatrix analysis for each polypeptide as follows: the signature region found in the indicated polypeptide sequences, the description of the signature, the eMatrix p-value(s) and the position(s) of the signature within the polypeptide sequence.

Using the pFam software program (Sonnhammer et al., Nucleic Acids Res., Vol. 26(1) pp. 320-322 (1998) herein incorporated by reference) all the polypeptide sequences were examined for domains with homology to certain peptide domains. The attached Sequence Listing provides the results obtained by PFAM analysis for each peptide, namely: the name of the domain found, the description, the p-value and the pFam score for the identified domain within the sequence.

Tables 1 and 2 follow. Table 1 shows the various tissue sources of SEQ ID NO: 1-30368. Table 2 shows the start and stop nucleotides for the translated amino acid sequence for which each assemblage encodes. Table 2 also provides a correlation between the amino acid sequences set forth in the Sequence Listing, the nucleotide sequences set forth in the Sequence Listing and the SEQ ID NO: in USSN 09/540,217

WHAT IS CLAIMED IS:

1. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of SEQ ID NO: 1-30368, a mature protein coding portion of SEQ ID NO: 1-30368, an active domain of SEQ ID NO: 1-30368, and complementary sequences thereof.

2. An isolated polynucleotide encoding a polypeptide with biological activity, wherein said polynucleotide hybridizes to the polynucleotide of claim 1 under stringent hybridization conditions.

3. An isolated polynucleotide encoding a polypeptide with biological activity, wherein said polynucleotide has greater than about 90% sequence identity with the polynucleotide of claim 1.

4. The polynucleotide of claim 1 wherein said polynucleotide is DNA.

5. An isolated polynucleotide of claim 1 wherein said polynucleotide comprises the complementary sequences.

6. A vector comprising the polynucleotide of claim 1.

7. An expression vector comprising the polynucleotide of claim 1.

8. A host cell genetically engineered to comprise the polynucleotide of claim 1.

9. A host cell genetically engineered to comprise the polynucleotide of claim 1 operatively associated with a regulatory sequence that modulates expression of the polynucleotide in the host cell.

10. An isolated polypeptide, wherein the polypeptide is selected from the group consisting of:
   (a) a polypeptide encoded by any one of the polynucleotides of claim 1; and
   (b) a polypeptide encoded by a polynucleotide hybridizing under stringent conditions with any one of SEQ ID NO: 1-30368.

11. A composition comprising the polypeptide of claim 10 and a carrier.

12. An antibody directed against the polypeptide of claim 10.

13. A method for detecting the polynucleotide of claim 1 in a sample, comprising:

a) contacting the sample with a compound that binds to and forms a complex with the polynucleotide of claim 1 for a period sufficient to form the complex; and

b) detecting the complex, so that if a complex is detected, the polynucleotide of claim 1 is detected.

14. A method for detecting the polynucleotide of claim 1 in a sample, comprising:

a) contacting the sample under stringent hybridization conditions with nucleic acid primers that anneal to the polynucleotide of claim 1 under such conditions;

b) amplifying a product comprising at least a portion of the polynucleotide of claim 1; and

c) detecting said product and thereby the polynucleotide of claim 1 in the sample.

15. The method of claim 14, wherein the polynucleotide is an RNA molecule and the method further comprises reverse transcribing an annealed RNA molecule into a cDNA polynucleotide.

16. A method for detecting the polypeptide of claim 10 in a sample, comprising:

a) contacting the sample with a compound that binds to and forms a complex with the polypeptide under conditions and for a period sufficient to form the complex; and

b) detecting formation of the complex, so that if a complex formation is detected, the polypeptide of claim 10 is detected.

17. A method for identifying a compound that binds to the polypeptide of claim 10, comprising:

a) contacting the compound with the polypeptide of claim 10 under conditions sufficient to form a polypeptide/compound complex; and

b) detecting the complex, so that if the polypeptide/compound complex is detected, a compound that binds to the polypeptide of claim 10 is identified.

18. A method for identifying a compound that binds to the polypeptide of claim 10, comprising:

a) contacting the compound with the polypeptide of claim 10, in a cell, under conditions sufficient to form a polypeptide/compound complex, wherein the complex drives expression of a reporter gene sequence in the cell; and

b) detecting the complex by detecting reporter gene sequence expression, so that if the polypeptide/compound complex is detected, a compound that binds to the polypeptide of claim 10 is identified.

19. A method of producing the polypeptide of claim 10, comprising,

a) culturing a host cell comprising a polynucleotide sequence selected from the group consisting of a polynucleotide sequence of SEQ ID NO: 1-30368, a mature protein coding portion of SEQ ID NO: 1-30368, an active domain of SEQ ID NO: 1-30368, complementary sequences thereof and a polynucleotide sequence hybridizing under stringent conditions to SEQ ID NO: 1-30368, under conditions sufficient to express the polypeptide in said cell; and

b) isolating the polypeptide from the cell culture or cells of step (a).

20. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 30369-60736, the mature protein portion thereof, or the active domain thereof.

21 The polypeptide of claim 20 wherein the polypeptide is provided on a polypeptide array.

22. A collection of polynucleotides, wherein the collection comprises the sequence information of at least one of SEQ ID NO: 1-30368.

23. The collection of claim 22, wherein the collection is provided on a nucleic acid array.

24. The collection of claim 23, wherein the array detects full-matches to any one of the polynucleotides in the collection.

25. The collection of claim 23, wherein the array detects mismatches to any one of the polynucleotides in the collection.

26. The collection of claim 22, wherein the collection is provided in a computer-readable format.

27. A method of treatment comprising administering to a mammalian subject in need thereof a therapeutic amount of a composition comprising a polypeptide of claim 10 or 20 and a pharmaceutically acceptable carrier.

28 A method of treatment comprising administering to a mammalian subject in need thereof a therapeutic amount of a composition comprising an antibody that specifically binds to a polypeptide of claim 10 or 20 and a pharmaceutically acceptable carrier.

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(54) Title: NOVEL NUCLEIC ACIDS AND POLYPEPTIDES

(57) Abstract: The present invention provides novel nucleic acids, novel polypeptide sequences encoded by these nucleic acids and uses thereof.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US01/08631

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12N 15/00, 15/12
US CL : 536/23.1, 23.5; 435/6, 320.1, 325

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 536/23.1, 23.5; 435/6, 320.1, 325

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
NONE

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
NONE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X, P --- A	Database Genbank. Accession No AL135937, 15 March 2001 (15.03.2001), particularly nucleotides 29925 through 30325.	1-8 ----------- 9, 19
X --- A	Database Genbank. Accession No. AA004350, HILLIER et al., Generation and analyhsis of 280,000 Human Expressed Sequence Tags. Genome Res. 07 May 1997 (07.05.1997), Vol. 6, No. 9, pages 807-828.	1-8 ----------- 9, 19

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
23 October 2001 (23.10.2001)	02 JAN 2002

Name and mailing address of the ISA/US	Authorized officer
Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Marianne P. Allen
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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US01/08631

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-9 and 19 with respect to SEQ ID NO: 1

Remark on Protest ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US01/08631

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-9 and 19, drawn to polynucleotides.

Group II, claim(s) 10-11, drawn to polypeptides.

Group III, claim(s) 12, drawn to antibodies.

Group IV, claim(s) 13-15, drawn to methods of detecting polynucleotides.

Group V, claim(s) 16, drawn to methods of detecting polypeptides.

Group VI, claim(s) 17, drawn to a first method of identifying compounds that bind.

Group VII, claim(s) 18, drawn to a second method of identifying compounds that bind.

Group VIII, claim(s) 20-21, drawn to polypeptide arrays.

Group IX, claim(s) 22-26, drawn to polynucleotide arrays.

Group X, claim(s) 27, drawn to a method of treatment using a polypeptide.

Group XI, claim(s) 28, drawn to a method of treatment using an antibody.

In addition, each of the SEQ ID NOS. named in the groups is considered to be a separate invention and applicant must elect a single SEQ ID NO. or for Groups VIII and IX a specific combination of SEQ ID NOS. for searching. Due to the burden of search for sequences, only a single SEQ ID NO. or specific combination of SEQ ID NOS. for Groups VIII and IX is considered to meet unity of invention.

The inventions listed as Groups I-XI do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Each of the products of Groups I-III, VIII, and IX differ structurally and functionally and thus lack the same or corresponding special technical feature. Each of the methods of Groups IV-VII, X and XI have different starting materials, method steps, and goals and thus lack the same or corresponding special technical feature.

As each SEQ ID NO. does not appear to share a common core structure, they are considered to be structurally and functionally distinct invention.

The number of inventions has been determined as follows. Each of groups I-XI is directed to 30368 SEQ ID NOS. As such, 30368 SEQ ID NOS. X 11 groups results in 334048 inventions.

If no additional fees are paid, Group I, claims 1-9 and 19, will be searched with respect to SEQ ID NO: 1. If Group VIII is elected, the default polypeptide array is considered to be an array comprising all of SEQ ID NOS. 30369-60736. If Group IX is elected, the default polynucleotide array is considered to be an array comprising all of SEQ ID NOS. 1-30368. Applicant is advised that they should specifically identify each additional group and each additional SEQ ID NO. being paid for. With respect to Groups VIII and IX, applicant should specifically identify each subset of SEQ ID NOS. present on the arrays if additional combinations are to be searched.

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WO 01/075067 A3

(54) Title: NOVEL NUCLEIC ACIDS AND POLYPEPTIDES

(57) Abstract: The present invention provides novel nucleic acids, novel polypeptide sequences encoded by these nucleic acids and uses thereof.

NOVEL NUCLEIC ACIDS AND POLYPEPTIDES

1. TECHNICAL FIELD

The present invention provides novel polynucleotides and proteins encoded by such polynucleotides, along with uses for these polynucleotides and proteins, for example in therapeutic, diagnostic and research methods.

2. BACKGROUND

Technology aimed at the discovery of protein factors (including *e.g.*, cytokines, such as lymphokines, interferons, CSFs, chemokines, and interleukins) has matured rapidly over the past decade. The now routine hybridization cloning and expression cloning techniques clone novel polynucleotides "directly" in the sense that they rely on information directly related to the discovered protein (*i.e.*, partial DNA/amino acid sequence of the protein in the case of hybridization cloning; activity of the protein in the case of expression cloning). More recent "indirect" cloning techniques such as signal sequence cloning, which isolates DNA sequences based on the presence of a now well-recognized secretory leader sequence motif, as well as various PCR-based or low stringency hybridization-based cloning techniques, have advanced the state of the art by making available large numbers of DNA/amino acid sequences for proteins that are known to have biological activity, for example, by virtue of their secreted nature in the case of leader sequence cloning, by virtue of their cell or tissue source in the case of PCR-based techniques, or by virtue of structural similarity to other genes of known biological activity.

Identified polynucleotide and polypeptide sequences have numerous applications in, for example, diagnostics, forensics, gene mapping; identification of mutations responsible for genetic disorders or other traits, to assess biodiversity, and to produce many other types of data and products dependent on DNA and amino acid sequences.

3. SUMMARY OF THE INVENTION

The compositions of the present invention include novel isolated polypeptides, novel isolated polynucleotides encoding such polypeptides, including recombinant DNA molecules, cloned genes or degenerate variants thereof, especially naturally occurring variants such as allelic variants, antisense polynucleotide molecules, and antibodies that specifically recognize one or more epitopes present on such polypeptides, as well as hybridomas producing such antibodies.

The compositions of the present invention additionally include vectors, including expression vectors, containing the polynucleotides of the invention, cells genetically engineered to contain such polynucleotides and cells genetically engineered to express such polynucleotides.

The present invention relates to a collection or library of at least one novel nucleic acid sequence assembled from expressed sequence tags (ESTs) isolated mainly by sequencing by hybridization (SBH), and in some cases, sequences obtained from one or more public databases. The invention relates also to the proteins encoded by such polynucleotides, along with therapeutic, diagnostic and research utilities for these polynucleotides and proteins. These nucleic acid sequences are designated as SEQ ID NO: 1-30368. The polypeptides sequences are designated SEQ ID NO: 30369-60736. The nucleic acids and polypeptides are provided in the Sequence Listing. In the nucleic acids provided in the Sequence Listing, A is adenosine; C is cytosine; G is guanine; T is thymine; and N is any of the four bases. In the amino acids provided in the Sequence Listing, * corresponds to the stop codon.

The nucleic acid sequences of the present invention also include, nucleic acid sequences that hybridize to the complement of SEQ ID NO: 1-30368 under stringent hybridization conditions; nucleic acid sequences which are allelic variants or species homologues of any of the nucleic acid sequences recited above, or nucleic acid sequences that encode a peptide comprising a specific domain or truncation of the peptides encoded by SEQ ID NO: 1-30368. A polynucleotide comprising a nucleotide sequence having at least 90% identity to an identifying sequence of SEQ ID NO: 1-30368 or a degenerate variant or fragment thereof. The identifying sequence can be 100 base pairs in length.

The nucleic acid sequences of the present invention also include the sequence information from the nucleic acid sequences of SEQ ID NO: 1-30368. The sequence information can be a segment of any one of SEQ ID NO: 1-30368 that uniquely identifies or represents the sequence information of SEQ ID NO: 1-30368.

A collection as used in this application can be a collection of only one polynucleotide. The collection of sequence information or identifying information of each sequence can be provided on a nucleic acid array. In one embodiment, segments of sequence information is provided on a nucleic acid array to detect the polynucleotide that contains the segment. The array can be designed to detect full-match or mismatch to the polynucleotide that contains the segment. The collection can also be provided in a computer-readable format.

This invention also includes the reverse or direct complement of any of the nucleic acid sequences recited above; cloning or expression vectors containing the nucleic acid sequences; and host cells or organisms transformed with these expression vectors. Nucleic acid sequences (or their reverse or direct complements) according to the invention have numerous applications in a variety of techniques known to those skilled in the art of molecular biology, such as use as hybridization probes, use as primers for PCR, use in an array, use in computer-readable media, use in sequencing

full-length genes, use for chromosome and gene mapping, use in the recombinant production of protein, and use in the generation of anti-sense DNA or RNA, their chemical analogs and the like.

In a preferred embodiment, the nucleic acid sequences of SEQ ID NO: 1-30368 or novel segments or parts of the nucleic acids of the invention are used as primers in expression assays that are well known in the art. In a particularly preferred embodiment, the nucleic acid sequences of SEQ ID NO: 1-30368 or novel segments or parts of the nucleic acids provided herein are used in diagnostics for identifying expressed genes or, as well known in the art and exemplified by Vollrath et al., Science 258:52-59 (1992), as expressed sequence tags for physical mapping of the human genome.

The isolated polynucleotides of the invention include, but are not limited to, a polynucleotide comprising any one of the nucleotide sequences set forth in SEQ ID NO: 1-30368; a polynucleotide comprising any of the full length protein coding sequences of SEQ ID NO: 1-30368; and a polynucleotide comprising any of the nucleotide sequences of the mature protein coding sequences of SEQ ID NO: 1-30368. The polynucleotides of the present invention also include, but are not limited to, a polynucleotide that hybridizes under stringent hybridization conditions to (a) the complement of any one of the nucleotide sequences set forth in SEQ ID NO: 1-30368; (b) a nucleotide sequence encoding any one of the amino acid sequences set forth in the Sequence Listing (*e.g.*, SEQ ID NO: 30369-60736); (c) a polynucleotide which is an allelic variant of any polynucleotides recited above; (d) a polynucleotide which encodes a species homolog (*e.g.* orthologs) of any of the proteins recited above; or (e) a polynucleotide that encodes a polypeptide comprising a specific domain or truncation of any of the polypeptides comprising an amino acid sequence set forth in the Sequence Listing.

The isolated polypeptides of the invention include, but are not limited to, a polypeptide comprising any of the amino acid sequences set forth in the Sequence Listing; or the corresponding full length or mature protein. Polypeptides of the invention also include polypeptides with biological activity that are encoded by (a) any of the polynucleotides having a nucleotide sequence set forth in SEQ ID NO: 1-30368; or (b) polynucleotides that hybridize to the complement of the polynucleotides of (a) under stringent hybridization conditions. Biologically or immunologically active variants of any of the polypeptide sequences in the Sequence Listing, and "substantial equivalents" thereof (*e.g.*, with at least about 65%, 70%, 75%, 80%, 85%, 90%, 95%, 98% or 99% amino acid sequence identity) that preferably retain biological activity are also contemplated. The polypeptides of the invention may be wholly or partially chemically synthesized but are preferably produced by recombinant means using the genetically engineered cells (*e.g.* host cells) of the invention.

The invention also provides compositions comprising a polypeptide of the invention. Polypeptide compositions of the invention may further comprise an acceptable carrier, such as a hydrophilic, *e.g.*, pharmaceutically acceptable, carrier.

The invention also provides host cells transformed or transfected with a polynucleotide of the invention.

The invention also relates to methods for producing a polypeptide of the invention comprising growing a culture of the host cells of the invention in a suitable culture medium under conditions permitting expression of the desired polypeptide, and purifying the polypeptide from the culture or from the host cells. Preferred embodiments include those in which the protein produced by such process is a mature form of the protein.

Polynucleotides according to the invention have numerous applications in a variety of techniques known to those skilled in the art of molecular biology. These techniques include use as hybridization probes, use as oligomers, or primers, for PCR, use for chromosome and gene mapping, use in the recombinant production of protein, and use in generation of anti-sense DNA or RNA, their chemical analogs and the like. For example, when the expression of an mRNA is largely restricted to a particular cell or tissue type, polynucleotides of the invention can be used as hybridization probes to detect the presence of the particular cell or tissue mRNA in a sample using, *e.g.*, *in situ* hybridization.

In other exemplary embodiments, the polynucleotides are used in diagnostics as expressed sequence tags for identifying expressed genes or, as well known in the art and exemplified by Vollrath et al., Science 258:52-59 (1992), as expressed sequence tags for physical mapping of the human genome.

The polypeptides according to the invention can be used in a variety of conventional procedures and methods that are currently applied to other proteins. For example, a polypeptide of the invention can be used to generate an antibody that specifically binds the polypeptide. Such antibodies, particularly monoclonal antibodies, are useful for detecting or quantitating the polypeptide in tissue. The polypeptides of the invention can also be used as molecular weight markers, and as a food supplement.

Methods are also provided for preventing, treating, or ameliorating a medical condition which comprises the step of administering to a mammalian subject a therapeutically effective amount of a composition comprising a polypeptide of the present invention and a pharmaceutically acceptable carrier.

In particular, the polypeptides and polynucleotides of the invention can be utilized, for example, in methods for the prevention and/or treatment of disorders involving aberrant protein expression or biological activity.

The present invention further relates to methods for detecting the presence of the polynucleotides or polypeptides of the invention in a sample. Such methods can, for example, be utilized as part of prognostic and diagnostic evaluation of disorders as recited herein and for the identification of subjects exhibiting a predisposition to such conditions. The invention provides a method for detecting the polynucleotides of the invention in a sample, comprising contacting the sample with a compound that binds to and forms a complex with the polynucleotide of interest for a period sufficient to form the complex and under conditions sufficient to form a complex and detecting the complex such that if a complex is detected, the polynucleotide of interest is detected. The invention also provides a method for detecting the polypeptides of the invention in a sample comprising contacting the sample with a compound that binds to and forms a complex with the polypeptide under conditions and for a period sufficient to form the complex and detecting the formation of the complex such that if a complex is formed, the polypeptide is detected.

The invention also provides kits comprising polynucleotide probes and/or monoclonal antibodies, and optionally quantitative standards, for carrying out methods of the invention. Furthermore, the invention provides methods for evaluating the efficacy of drugs, and monitoring the progress of patients, involved in clinical trials for the treatment of disorders as recited above.

The invention also provides methods for the identification of compounds that modulate (*i.e.*, increase or decrease) the expression or activity of the polynucleotides and/or polypeptides of the invention. Such methods can be utilized, for example, for the identification of compounds that can ameliorate symptoms of disorders as recited herein. Such methods can include, but are not limited to, assays for identifying compounds and other substances that interact with (*e.g.*, bind to) the polypeptides of the invention. The invention provides a method for identifying a compound that binds to the polypeptides of the invention comprising contacting the compound with a polypeptide of the invention in a cell for a time sufficient to form a polypeptide/compound complex, wherein the complex drives expression of a reporter gene sequence in the cell; and detecting the complex by detecting the reporter gene sequence expression such that if expression of the reporter gene is detected the compound that binds to a polypeptide of the invention is identified.

The methods of the invention also provides methods for treatment which involve the administration of the polynucleotides or polypeptides of the invention to individuals exhibiting symptoms or tendencies. In addition, the invention encompasses methods for treating diseases or disorders as recited herein comprising administering compounds and other substances that modulate the overall activity of the target gene products. Compounds and other substances can

effect such modulation either on the level of target gene/protein expression or target protein activity.

The polypeptides of the present invention and the polynucleotides encoding them are also useful for the same functions known to one of skill in the art as the polypeptides and polynucleotides to which they have homology (set forth in the sequence listing). If no homology is set forth for a sequence, then the polypeptides and polynucleotides of the present invention are useful for a variety of applications, as described herein, including use in arrays for detection.

4. DETAILED DESCRIPTION OF THE INVENTION

4.1 DEFINITIONS

It must be noted that as used herein and in the appended claims, the singular forms “a”, “an” and “the” include plural references unless the context clearly dictates otherwise.

The term "active" refers to those forms of the polypeptide which retain the biologic and/or immunologic activities of any naturally occurring polypeptide. According to the invention, the terms “biologically active” or “biological activity” refer to a protein or peptide having structural, regulatory or biochemical functions of a naturally occurring molecule. Likewise “immunologically active” or “immunological activity” refers to the capability of the natural, recombinant or synthetic polypeptide to induce a specific immune response in appropriate animals or cells and to bind with specific antibodies.

The term "activated cells” as used in this application are those cells which are engaged in extracellular or intracellular membrane trafficking, including the export of secretory or enzymatic molecules as part of a normal or disease process.

The terms “complementary” or “complementarity” refer to the natural binding of polynucleotides by base pairing. For example, the sequence 5’-AGT-3’ binds to the complementary sequence 3’-TCA-5’. Complementarity between two single-stranded molecules may be “partial” such that only some of the nucleic acids bind or it may be “complete” such that total complementarity exists between the single stranded molecules. The degree of complementarity between the nucleic acid strands has significant effects on the efficiency and strength of the hybridization between the nucleic acid strands.

The term “embryonic stem cells (ES)” refers to a cell that can give rise to many differentiated cell types in an embryo or an adult, including the germ cells. The term “germ line stem cells (GSCs)” refers to stem cells derived from primordial stem cells that provide a steady and continuous source of germ cells for the production of gametes. The term “primordial germ

cells (PGCs)" refers to a small population of cells set aside from other cell lineages particularly from the yolk sac, mesenteries, or gonadal ridges during embryogenesis that have the potential to differentiate into germ cells and other cells. PGCs are the source from which GSCs and ES cells are derived The PGCs, the GSCs and the ES cells are capable of self-renewal. Thus these cells not only populate the germ line and give rise to a plurality of terminally differentiated cells that comprise the adult specialized organs, but are able to regenerate themselves.

The term "expression modulating fragment," EMF, means a series of nucleotides which modulates the expression of an operably linked ORF or another EMF.

As used herein, a sequence is said to "modulate the expression of an operably linked sequence" when the expression of the sequence is altered by the presence of the EMF. EMFs include, but are not limited to, promoters, and promoter modulating sequences (inducible elements). One class of EMFs are nucleic acid fragments which induce the expression of an operably linked ORF in response to a specific regulatory factor or physiological event.

The terms "nucleotide sequence" or "nucleic acid" or "polynucleotide" or "oligonucleotide" are used interchangeably and refer to a heteropolymer of nucleotides or the sequence of these nucleotides. These phrases also refer to DNA or RNA of genomic or synthetic origin which may be single-stranded or double-stranded and may represent the sense or the antisense strand, to peptide nucleic acid (PNA) or to any DNA-like or RNA-like material. In the sequences herein A is adenine, C is cytosine, T is thymine, G is guanine and N is A, C, G or T (U). It is contemplated that where the polynucleotide is RNA, the T (thymine) in the sequences provided herein is substituted with U (uracil). Generally, nucleic acid segments provided by this invention may be assembled from fragments of the genome and short oligonucleotide linkers, or from a series of oligonucleotides, or from individual nucleotides, to provide a synthetic nucleic acid which is capable of being expressed in a recombinant transcriptional unit comprising regulatory elements derived from a microbial or viral operon, or a eukaryotic gene.

The terms "oligonucleotide fragment" or a "polynucleotide fragment", "portion," or "segment" or "probe" or "primer" are used interchangeably and refer to a sequence of nucleotide residues which are at least about 5 nucleotides, more preferably at least about 7 nucleotides, more preferably at least about 9 nucleotides, more preferably at least about 11 nucleotides and most preferably at least about 17 nucleotides. The fragment is preferably less than about 500 nucleotides, preferably less than about 200 nucleotides, more preferably less than about 100 nucleotides, more preferably less than about 50 nucleotides and most preferably less than 30 nucleotides. Preferably the probe is from about 6 nucleotides to about 200 nucleotides, preferably from about 15 to about 50 nucleotides, more preferably from about 17 to 30 nucleotides and most preferably from about 20 to 25 nucleotides. Preferably the fragments can

be used in polymerase chain reaction (PCR), various hybridization procedures or microarray procedures to identify or amplify identical or related parts of mRNA or DNA molecules. A fragment or segment may uniquely identify each polynucleotide sequence of the present invention. Preferably the fragment comprises a sequence substantially similar to any one of SEQ ID NO: 1-30368.

Probes may, for example, be used to determine whether specific mRNA molecules are present in a cell or tissue or to isolate similar nucleic acid sequences from chromosomal DNA as described by Walsh et al. (Walsh, P.S. et al., 1992, PCR Methods Appl 1:241-250). They may be labeled by nick translation, Klenow fill-in reaction, PCR, or other methods well known in the art. Probes of the present invention, their preparation and/or labeling are elaborated in Sambrook, J. et al., 1989, Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, NY; or Ausubel, F.M. et al., 1989, Current Protocols in Molecular Biology, John Wiley & Sons, New York NY, both of which are incorporated herein by reference in their entirety.

The nucleic acid sequences of the present invention also include the sequence information from the nucleic acid sequences of SEQ ID NO: 1-30368. The sequence information can be a segment of any one of SEQ ID NO: 1-30368 that uniquely identifies or represents the sequence information of that sequence of SEQ ID NO: 1-30368. One such segment can be a twenty-mer nucleic acid sequence because the probability that a twenty-mer is fully matched in the human genome is 1 in 300. In the human genome, there are three billion base pairs in one set of chromosomes. Because 4^{20} possible twenty-mers exist, there are 300 times more twenty-mers than there are base pairs in a set of human chromosomes. Using the same analysis, the probability for a seventeen-mer to be fully matched in the human genome is approximately 1 in 5. When these segments are used in arrays for expression studies, fifteen-mer segments can be used. The probability that the fifteen-mer is fully matched in the expressed sequences is also approximately one in five because expressed sequences comprise less than approximately 5% of the entire genome sequence.

Similarly, when using sequence information for detecting a single mismatch, a segment can be a twenty-five mer. The probability that the twenty-five mer would appear in a human genome with a single mismatch is calculated by multiplying the probability for a full match ($1 \div 4^{25}$) times the increased probability for mismatch at each nucleotide position (3×25). The probability that an eighteen mer with a single mismatch can be detected in an array for expression studies is approximately one in five. The probability that a twenty-mer with a single mismatch can be detected in a human genome is approximately one in five.

The term "open reading frame," ORF, means a series of nucleotide triplets coding for amino acids without any termination codons and is a sequence translatable into protein.

The terms “operably linked” or “operably associated” refer to functionally related nucleic acid sequences. For example, a promoter is operably associated or operably linked with a coding sequence if the promoter controls the transcription of the coding sequence. While operably linked nucleic acid sequences can be contiguous and in the same reading frame, certain genetic elements *e.g.* repressor genes are not contiguously linked to the coding sequence but still control transcription/translation of the coding sequence.

The term “pluripotent” refers to the capability of a cell to differentiate into a number of differentiated cell types that are present in an adult organism. A pluripotent cell is restricted in its differentiation capability in comparison to a totipotent cell.

The terms “polypeptide” or “peptide” or “amino acid sequence” refer to an oligopeptide, peptide, polypeptide or protein sequence or fragment thereof and to naturally occurring or synthetic molecules. A polypeptide "fragment," "portion," or "segment" is a stretch of amino acid residues of at least about 5 amino acids, preferably at least about 7 amino acids, more preferably at least about 9 amino acids and most preferably at least about 17 or more amino acids. The peptide preferably is not greater than about 200 amino acids, more preferably less than 150 amino acids and most preferably less than 100 amino acids. Preferably the peptide is from about 5 to about 200 amino acids. To be active, any polypeptide must have sufficient length to display biological and/or immunological activity.

The term "naturally occurring polypeptide" refers to polypeptides produced by cells that have not been genetically engineered and specifically contemplates various polypeptides arising from post-translational modifications of the polypeptide including, but not limited to, acetylation, carboxylation, glycosylation, phosphorylation, lipidation and acylation.

The term “translated protein coding portion” means a sequence which encodes for the full length protein which may include any leader sequence or any processing sequence.

The term “mature protein coding sequence” means a sequence which encodes a peptide or protein without a signal or leader sequence. The “mature protein portion” means that portion of the protein which does not include a signal or leader sequence. The peptide may have been produced by processing in the cell which removes any leader/signal sequence. The mature protein portion may or may not include an initial methionine residue. The methionine residue may be removed from the protein during processing in the cell. The peptide may be produced synthetically or the protein may have been produced using a polynucleotide only encoding for the mature protein coding sequence.

The term "derivative" refers to polypeptides chemically modified by such techniques as ubiquitination, labeling (*e.g.*, with radionuclides or various enzymes), covalent polymer attachment such as pegylation (derivatization with polyethylene glycol) and insertion or substitution by chemical synthesis of amino acids such as ornithine, which do not normally occur in human proteins.

The term "variant"(or "analog") refers to any polypeptide differing from naturally occurring polypeptides by amino acid insertions, deletions, and substitutions, created using, *e.g.*, recombinant DNA techniques. Guidance in determining which amino acid residues may be replaced, added or deleted without abolishing activities of interest, may be found by comparing the sequence of the particular polypeptide with that of homologous peptides and minimizing the number of amino acid sequence changes made in regions of high homology (conserved regions) or by replacing amino acids with consensus sequence.

Alternatively, recombinant variants encoding these same or similar polypeptides may be synthesized or selected by making use of the "redundancy" in the genetic code. Various codon substitutions, such as the silent changes which produce various restriction sites, may be introduced to optimize cloning into a plasmid or viral vector or expression in a particular prokaryotic or eukaryotic system. Mutations in the polynucleotide sequence may be reflected in the polypeptide or domains of other peptides added to the polypeptide to modify the properties of any part of the polypeptide, to change characteristics such as ligand-binding affinities, interchain affinities, or degradation/turnover rate.

Preferably, amino acid "substitutions" are the result of replacing one amino acid with another amino acid having similar structural and/or chemical properties, *i.e.*, conservative amino acid replacements. "Conservative" amino acid substitutions may be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity, and/or the amphipathic nature of the residues involved. For example, nonpolar (hydrophobic) amino acids include alanine, leucine, isoleucine, valine, proline, phenylalanine, tryptophan, and methionine; polar neutral amino acids include glycine, serine, threonine, cysteine, tyrosine, asparagine, and glutamine; positively charged (basic) amino acids include arginine, lysine, and histidine; and negatively charged (acidic) amino acids include aspartic acid and glutamic acid. "Insertions" or "deletions" are preferably in the range of about 1 to 20 amino acids, more preferably 1 to 10 amino acids. The variation allowed may be experimentally determined by systematically making insertions, deletions, or substitutions of amino acids in a polypeptide molecule using recombinant DNA techniques and assaying the resulting recombinant variants for activity.

Alternatively, where alteration of function is desired, insertions, deletions or non-conservative alterations can be engineered to produce altered polypeptides. Such alterations

can, for example, alter one or more of the biological functions or biochemical characteristics of the polypeptides of the invention. For example, such alterations may change polypeptide characteristics such as ligand-binding affinities, interchain affinities, or degradation/turnover rate. Further, such alterations can be selected so as to generate polypeptides that are better suited for expression, scale up and the like in the host cells chosen for expression. For example, cysteine residues can be deleted or substituted with another amino acid residue in order to eliminate disulfide bridges.

The terms "purified" or "substantially purified" as used herein denotes that the indicated nucleic acid or polypeptide is present in the substantial absence of other biological macromolecules, *e.g.*, polynucleotides, proteins, and the like. In one embodiment, the polynucleotide or polypeptide is purified such that it constitutes at least 95% by weight, more preferably at least 99% by weight, of the indicated biological macromolecules present (but water, buffers, and other small molecules, especially molecules having a molecular weight of less than 1000 daltons, can be present).

The term "isolated" as used herein refers to a nucleic acid or polypeptide separated from at least one other component (*e.g.*, nucleic acid or polypeptide) present with the nucleic acid or polypeptide in its natural source. In one embodiment, the nucleic acid or polypeptide is found in the presence of (if anything) only a solvent, buffer, ion, or other component normally present in a solution of the same. The terms "isolated" and "purified" do not encompass nucleic acids or polypeptides present in their natural source.

The term "recombinant," when used herein to refer to a polypeptide or protein, means that a polypeptide or protein is derived from recombinant (*e.g.*, microbial, insect, or mammalian) expression systems. "Microbial" refers to recombinant polypeptides or proteins made in bacterial or fungal (*e.g.*, yeast) expression systems. As a product, "recombinant microbial" defines a polypeptide or protein essentially free of native endogenous substances and unaccompanied by associated native glycosylation. Polypeptides or proteins expressed in most bacterial cultures, *e.g.*, *E. coli*, will be free of glycosylation modifications; polypeptides or proteins expressed in yeast will have a glycosylation pattern in general different from those expressed in mammalian cells.

The term "recombinant expression vehicle or vector" refers to a plasmid or phage or virus or vector, for expressing a polypeptide from a DNA (RNA) sequence. An expression vehicle can comprise a transcriptional unit comprising an assembly of (1) a genetic element or elements having a regulatory role in gene expression, for example, promoters or enhancers, (2) a structural or coding sequence which is transcribed into mRNA and translated into protein, and (3) appropriate transcription initiation and termination sequences. Structural units intended for use

in yeast or eukaryotic expression systems preferably include a leader sequence enabling extracellular secretion of translated protein by a host cell. Alternatively, where recombinant protein is expressed without a leader or transport sequence, it may include an amino terminal methionine residue. This residue may or may not be subsequently cleaved from the expressed recombinant protein to provide a final product.

The term "recombinant expression system" means host cells which have stably integrated a recombinant transcriptional unit into chromosomal DNA or carry the recombinant transcriptional unit extrachromosomally. Recombinant expression systems as defined herein will express heterologous polypeptides or proteins upon induction of the regulatory elements linked to the DNA segment or synthetic gene to be expressed. This term also means host cells which have stably integrated a recombinant genetic element or elements having a regulatory role in gene expression, for example, promoters or enhancers. Recombinant expression systems as defined herein will express polypeptides or proteins endogenous to the cell upon induction of the regulatory elements linked to the endogenous DNA segment or gene to be expressed. The cells can be prokaryotic or eukaryotic.

The term "secreted" includes a protein that is transported across or through a membrane, including transport as a result of signal sequences in its amino acid sequence when it is expressed in a suitable host cell. "Secreted" proteins include without limitation proteins secreted wholly (*e.g.*, soluble proteins) or partially (*e.g.*, receptors) from the cell in which they are expressed. "Secreted" proteins also include without limitation proteins that are transported across the membrane of the endoplasmic reticulum. "Secreted" proteins are also intended to include proteins containing non-typical signal sequences (*e.g.* Interleukin-1 Beta, see Krasney, P.A. and Young, P.R. (1992) Cytokine 4(2):134 -143) and factors released from damaged cells (*e.g.* Interleukin-1 Receptor Antagonist, see Arend, W.P. et. al. (1998) Annu. Rev. Immunol. 16:27-55)

Where desired, an expression vector may be designed to contain a "signal or leader sequence" which will direct the polypeptide through the membrane of a cell. Such a sequence may be naturally present on the polypeptides of the present invention or provided from heterologous protein sources by recombinant DNA techniques.

The term "stringent" is used to refer to conditions that are commonly understood in the art as stringent. Stringent conditions can include highly stringent conditions (*i.e.*, hybridization to filter-bound DNA in 0.5 M $NaHPO_4$, 7% sodium dodecyl sulfate (SDS), 1 mM EDTA at 65°C, and washing in 0.1X SSC/0.1% SDS at 68°C), and moderately stringent conditions (*i.e.*, washing in 0.2X SSC/0.1% SDS at 42°C). Other exemplary hybridization conditions are described herein in the examples.

In instances of hybridization of deoxyoligonucleotides, additional exemplary stringent hybridization conditions include washing in 6X SSC/0.05% sodium pyrophosphate at 37°C (for 14-base oligonucleotides), 48°C (for 17-base oligos), 55°C (for 20-base oligonucleotides), and 60°C (for 23-base oligonucleotides).

As used herein, "substantially equivalent" can refer both to nucleotide and amino acid sequences, for example a mutant sequence, that varies from a reference sequence by one or more substitutions, deletions, or additions, the net effect of which does not result in an adverse functional dissimilarity between the reference and subject sequences. Typically, such a substantially equivalent sequence varies from one of those listed herein by no more than about 35% (*i.e.*, the number of individual residue substitutions, additions, and/or deletions in a substantially equivalent sequence, as compared to the corresponding reference sequence, divided by the total number of residues in the substantially equivalent sequence is about 0.35 or less). Such a sequence is said to have 65% sequence identity to the listed sequence. In one embodiment, a substantially equivalent, *e.g.*, mutant, sequence of the invention varies from a listed sequence by no more than 30% (70% sequence identity); in a variation of this embodiment, by no more than 25% (75% sequence identity); and in a further variation of this embodiment, by no more than 20% (80% sequence identity) and in a further variation of this embodiment, by no more than 10% (90% sequence identity) and in a further variation of this embodiment, by no more that 5% (95% sequence identity). Substantially equivalent, *e.g.*, mutant, amino acid sequences according to the invention preferably have at least 80% sequence identity with a listed amino acid sequence, more preferably at least 85% sequence identity, more preferably at least 90% sequence identity, more preferably at least 95% identity, more preferably at least 98% identity, and most preferably at least 99% identity. Substantially equivalent nucleotide sequences of the invention can have lower percent sequence identities, taking into account, for example, the redundancy or degeneracy of the genetic code. Preferably, nucleotide sequence has at least about 65% identity, more preferably at least about 75% identity, more preferably at least about 80% sequence identity, more preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, and most preferably at least about 95% identity, more preferably at least about 98% sequence identity, and most preferably at least about 99% sequence identity. For the purposes of the present invention, sequences having substantially equivalent biological activity and substantially equivalent expression characteristics are considered substantially equivalent. For the purposes of determining equivalence, truncation of the mature sequence (*e.g.*, via a mutation which creates a spurious stop codon) should be disregarded. Sequence identity may be determined, *e.g.*, using the Jotun Hein method (Hein, J.

(1990) Methods Enzymol. 183:626-645). Identity between sequences can also be determined by other methods known in the art, *e.g.* by varying hybridization conditions.

The term "totipotent" refers to the capability of a cell to differentiate into all of the cell types of an adult organism.

The term "transformation" means introducing DNA into a suitable host cell so that the DNA is replicable, either as an extrachromosomal element, or by chromosomal integration. The term "transfection" refers to the taking up of an expression vector by a suitable host cell, whether or not any coding sequences are in fact expressed. The term "infection" refers to the introduction of nucleic acids into a suitable host cell by use of a virus or viral vector.

As used herein, an "uptake modulating fragment," UMF, means a series of nucleotides which mediate the uptake of a linked DNA fragment into a cell. UMFs can be readily identified using known UMFs as a target sequence or target motif with the computer-based systems described below. The presence and activity of a UMF can be confirmed by attaching the suspected UMF to a marker sequence. The resulting nucleic acid molecule is then incubated with an appropriate host under appropriate conditions and the uptake of the marker sequence is determined. As described above, a UMF will increase the frequency of uptake of a linked marker sequence.

Each of the above terms is meant to encompass all that is described for each, unless the context dictates otherwise.

4.2 NUCLEIC ACIDS OF THE INVENTION

Nucleotide sequences of the invention are set forth in the Sequence Listing.

The isolated polynucleotides of the invention include a polynucleotide comprising the nucleotide sequences of SEQ ID NO: 1-30368; a polynucleotide encoding any one of the peptide sequences of SEQ ID NO: 30369-60736; and a polynucleotide comprising the nucleotide sequence encoding the mature protein coding sequence of the polypeptides of any one of SEQ ID NO: 30369-60736. The polynucleotides of the present invention also include, but are not limited to, a polynucleotide that hybridizes under stringent conditions to (a) the complement of any of the nucleotides sequences of SEQ ID NO: 1-30368; (b) nucleotide sequences encoding any one of the amino acid sequences set forth in the Sequence Listing; (c) a polynucleotide which is an allelic variant of any polynucleotide recited above; (d) a polynucleotide which encodes a species homolog of any of the proteins recited above; or (e) a polynucleotide that encodes a polypeptide comprising a specific domain or truncation of the polypeptides of SEQ ID NO: 30369-60736. Domains of interest may depend on the nature of the encoded polypeptide; *e.g.*, domains in receptor-like polypeptides include ligand-binding, extracellular, transmembrane, or cytoplasmic

domains, or combinations thereof; domains in immunoglobulin-like proteins include the variable immunoglobulin-like domains; domains in enzyme-like polypeptides include catalytic and substrate binding domains; and domains in ligand polypeptides include receptor-binding domains.

The polynucleotides of the invention include naturally occurring or wholly or partially synthetic DNA, *e.g.*, cDNA and genomic DNA, and RNA, *e.g.*, mRNA. The polynucleotides may include all of the coding region of the cDNA or may represent a portion of the coding region of the cDNA.

The present invention also provides genes corresponding to the cDNA sequences disclosed herein. The corresponding genes can be isolated in accordance with known methods using the sequence information disclosed herein. Such methods include the preparation of probes or primers from the disclosed sequence information for identification and/or amplification of genes in appropriate genomic libraries or other sources of genomic materials. Further 5' and 3' sequence can be obtained using methods known in the art. For example, full length cDNA or genomic DNA that corresponds to any of the polynucleotides of SEQ ID NO: 1-30368 can be obtained by screening appropriate cDNA or genomic DNA libraries under suitable hybridization conditions using any of the polynucleotides of SEQ ID NO: 1-30368 or a portion thereof as a probe. Alternatively, the polynucleotides of SEQ ID NO: 1-30368 may be used as the basis for suitable primer(s) that allow identification and/or amplification of genes in appropriate genomic DNA or cDNA libraries.

The nucleic acid sequences of the invention can be assembled from ESTs and sequences (including cDNA and genomic sequences) obtained from one or more public databases, such as dbEST, gbpri, and UniGene. The EST sequences can provide identifying sequence information, representative fragment or segment information, or novel segment information for the full-length gene.

The polynucleotides of the invention also provide polynucleotides including nucleotide sequences that are substantially equivalent to the polynucleotides recited above. Polynucleotides according to the invention can have, *e.g.*, at least about 65%, at least about 70%, at least about 75%, at least about 80%, 81%, 82%, 83%, 84%, more typically at least about 85%, 86%, 87%, 88%, 89%, more typically at least about 90%, 91%, 92%, 93%, 94%, and even more typically at least about 95%, 96%, 97%, 98%, 99%, sequence identity to a polynucleotide recited above.

Included within the scope of the nucleic acid sequences of the invention are nucleic acid sequence fragments that hybridize under stringent conditions to any of the nucleotide sequences of SEQ ID NO: 1-30368, or complements thereof, which fragment is greater than about 5 nucleotides, preferably 7 nucleotides, more preferably greater than 9 nucleotides and most preferably greater than 17 nucleotides. Fragments of, *e.g.* 15, 17, or 20 nucleotides or more that

are selective for (*i.e.* specifically hybridize to any one of the polynucleotides of the invention) are contemplated. Probes capable of specifically hybridizing to a polynucleotide can differentiate polynucleotide sequences of the invention from other polynucleotide sequences in the same family of genes or can differentiate human genes from genes of other species, and are preferably based on unique nucleotide sequences.

The sequences falling within the scope of the present invention are not limited to these specific sequences, but also include allelic and species variations thereof. Allelic and species variations can be routinely determined by comparing the sequence provided in SEQ ID NO: 1-30368, a representative fragment thereof, or a nucleotide sequence at least 90% identical, preferably 95% identical, to SEQ ID NO: 1-30368 with a sequence from another isolate of the same species. Furthermore, to accommodate codon variability, the invention includes nucleic acid molecules coding for the same amino acid sequences as do the specific ORFs disclosed herein. In other words, in the coding region of an ORF, substitution of one codon for another codon that encodes the same amino acid is expressly contemplated.

The nearest neighbor or homology result for the nucleic acids of the present invention, including SEQ ID NO: 1-30368 can be obtained by searching a database using an algorithm or a program. Preferably, a BLAST which stands for Basic Local Alignment Search Tool is used to search for local sequence alignments (Altshul, S.F. J Mol. Evol. 36 290-300 (1993) and Altschul S.F. et al. J. Mol. Biol. 21:403-410 (1990)). Alternatively a FASTA version 3 search against Genpept, using Fastxy algorithm.

Species homologs (or orthologs) of the disclosed polynucleotides and proteins are also provided by the present invention. Species homologs may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source from the desired species.

The invention also encompasses allelic variants of the disclosed polynucleotides or proteins; that is, naturally occurring alternative forms of the isolated polynucleotide which also encode proteins which are identical, homologous or related to that encoded by the polynucleotides.

The nucleic acid sequences of the invention are further directed to sequences which encode variants of the described nucleic acids. These amino acid sequence variants may be prepared by methods known in the art by introducing appropriate nucleotide changes into a native or variant polynucleotide. There are two variables in the construction of amino acid sequence variants: the location of the mutation and the nature of the mutation. Nucleic acids encoding the amino acid sequence variants are preferably constructed by mutating the polynucleotide to encode an amino acid sequence that does not occur in nature. These nucleic

acid alterations can be made at sites that differ in the nucleic acids from different species (variable positions) or in highly conserved regions (constant regions). Sites at such locations will typically be modified in series, *e.g.*, by substituting first with conservative choices (*e.g.*, hydrophobic amino acid to a different hydrophobic amino acid) and then with more distant choices (*e.g.*, hydrophobic amino acid to a charged amino acid), and then deletions or insertions may be made at the target site. Amino acid sequence deletions generally range from about 1 to 30 residues, preferably about 1 to 10 residues, and are typically contiguous. Amino acid insertions include amino- and/or carboxyl-terminal fusions ranging in length from one to one hundred or more residues, as well as intrasequence insertions of single or multiple amino acid residues. Intrasequence insertions may range generally from about 1 to 10 amino residues, preferably from 1 to 5 residues. Examples of terminal insertions include the heterologous signal sequences necessary for secretion or for intracellular targeting in different host cells and sequences such as FLAG or poly-histidine sequences useful for purifying the expressed protein.

In a preferred method, polynucleotides encoding the novel amino acid sequences are changed via site-directed mutagenesis. This method uses oligonucleotide sequences to alter a polynucleotide to encode the desired amino acid variant, as well as sufficient adjacent nucleotides on both sides of the changed amino acid to form a stable duplex on either side of the site of being changed. In general, the techniques of site-directed mutagenesis are well known to those of skill in the art and this technique is exemplified by publications such as, Edelman et al., *DNA* 2:183 (1983). A versatile and efficient method for producing site-specific changes in a polynucleotide sequence was published by Zoller and Smith, *Nucleic Acids Res.* 10:6487-6500 (1982). PCR may also be used to create amino acid sequence variants of the novel nucleic acids. When small amounts of template DNA are used as starting material, primer(s) that differs slightly in sequence from the corresponding region in the template DNA can generate the desired amino acid variant. PCR amplification results in a population of product DNA fragments that differ from the polynucleotide template encoding the polypeptide at the position specified by the primer. The product DNA fragments replace the corresponding region in the plasmid and this gives a polynucleotide encoding the desired amino acid variant.

A further technique for generating amino acid variants is the cassette mutagenesis technique described in Wells et al., *Gene* 34:315 (1985); and other mutagenesis techniques well known in the art, such as, for example, the techniques in Sambrook et al., supra, and *Current Protocols in Molecular Biology*, Ausubel et al. Due to the inherent degeneracy of the genetic code, other DNA sequences which encode substantially the same or a functionally equivalent amino acid sequence may be used in the practice of the invention for the cloning and expression

of these novel nucleic acids. Such DNA sequences include those which are capable of hybridizing to the appropriate novel nucleic acid sequence under stringent conditions.

Polynucleotides encoding preferred polypeptide truncations of the invention can be used to generate polynucleotides encoding chimeric or fusion proteins comprising one or more domains of the invention and heterologous protein sequences.

The polynucleotides of the invention additionally include the complement of any of the polynucleotides recited above. The polynucleotide can be DNA (genomic, cDNA, amplified, or synthetic) or RNA. Methods and algorithms for obtaining such polynucleotides are well known to those of skill in the art and can include, for example, methods for determining hybridization conditions that can routinely isolate polynucleotides of the desired sequence identities.

In accordance with the invention, polynucleotide sequences comprising the mature protein coding sequences corresponding to any one of SEQ ID NO: 1-30368, or functional equivalents thereof, may be used to generate recombinant DNA molecules that direct the expression of that nucleic acid, or a functional equivalent thereof, in appropriate host cells. Also included are the cDNA inserts of any of the clones identified herein.

A polynucleotide according to the invention can be joined to any of a variety of other nucleotide sequences by well-established recombinant DNA techniques (see Sambrook J et al.. (1989) Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, NY). Useful nucleotide sequences for joining to polynucleotides include an assortment of vectors, *e.g.*, plasmids, cosmids, lambda phage derivatives, phagemids, and the like, that are well known in the art. Accordingly, the invention also provides a vector including a polynucleotide of the invention and a host cell containing the polynucleotide. In general, the vector contains an origin of replication functional in at least one organism, convenient restriction endonuclease sites, and a selectable marker for the host cell. Vectors according to the invention include expression vectors, replication vectors, probe generation vectors, and sequencing vectors. A host cell according to the invention can be a prokaryotic or eukaryotic cell and can be a unicellular organism or part of a multicellular organism.

The present invention further provides recombinant constructs comprising a nucleic acid having any of the nucleotide sequences of SEQ ID NO: 1-30368 or a fragment thereof or any other polynucleotides of the invention. In one embodiment, the recombinant constructs of the present invention comprise a vector, such as a plasmid or viral vector, into which a nucleic acid having any of the nucleotide sequences of SEQ ID NO: 1-30368 or a fragment thereof is inserted, in a forward or reverse orientation. In the case of a vector comprising one of the ORFs of the present invention, the vector may further comprise regulatory sequences, including for example, a promoter, operably linked to the ORF. Large numbers of suitable vectors and

promoters are known to those of skill in the art and are commercially available for generating the recombinant constructs of the present invention. The following vectors are provided by way of example. Bacterial: pBs, phagescript, PsiX174, pBluescript SK, pBs KS, pNH8a, pNH16a, pNH18a, pNH46a (Stratagene); pTrc99A, pKK223-3, pKK233-3, pDR540, pRIT5 (Pharmacia). Eukaryotic: pWLneo, pSV2cat, pOG44, PXTI, pSG (Stratagene) pSVK3, pBPV, pMSG, pSVL (Pharmacia).

The isolated polynucleotide of the invention may be operably linked to an expression control sequence such as the pMT2 or pED expression vectors disclosed in Kaufman et al., *Nucleic Acids Res.* 19, 4485-4490 (1991), in order to produce the protein recombinantly. Many suitable expression control sequences are known in the art. General methods of expressing recombinant proteins are also known and are exemplified in R. Kaufman, *Methods in Enzymology* 185, 537-566 (1990). As defined herein "operably linked" means that the isolated polynucleotide of the invention and an expression control sequence are situated within a vector or cell in such a way that the protein is expressed by a host cell which has been transformed (transfected) with the ligated polynucleotide/expression control sequence.

Promoter regions can be selected from any desired gene using CAT (chloramphenicol transferase) vectors or other vectors with selectable markers. Two appropriate vectors are pKK232-8 and pCM7. Particular named bacterial promoters include lacI, lacZ, T3, T7, gpt, lambda PR, and trc. Eukaryotic promoters include CMV immediate early, HSV thymidine kinase, early and late SV40, LTRs from retrovirus, and mouse metallothionein-I. Selection of the appropriate vector and promoter is well within the level of ordinary skill in the art. Generally, recombinant expression vectors will include origins of replication and selectable markers permitting transformation of the host cell, *e.g.*, the ampicillin resistance gene of *E. coli* and *S. cerevisiae* TRP1 gene, and a promoter derived from a highly-expressed gene to direct transcription of a downstream structural sequence. Such promoters can be derived from operons encoding glycolytic enzymes such as 3-phosphoglycerate kinase (PGK), a-factor, acid phosphatase, or heat shock proteins, among others. The heterologous structural sequence is assembled in appropriate phase with translation initiation and termination sequences, and preferably, a leader sequence capable of directing secretion of translated protein into the periplasmic space or extracellular medium. Optionally, the heterologous sequence can encode a fusion protein including an amino terminal identification peptide imparting desired characteristics, *e.g.*, stabilization or simplified purification of expressed recombinant product. Useful expression vectors for bacterial use are constructed by inserting a structural DNA sequence encoding a desired protein together with suitable translation initiation and termination signals in operable reading phase with a functional promoter. The vector will comprise one or

more phenotypic selectable markers and an origin of replication to ensure maintenance of the vector and to, if desirable, provide amplification within the host. Suitable prokaryotic hosts for transformation include *E. coli*, *Bacillus subtilis*, *Salmonella typhimurium* and various species within the genera *Pseudomonas*, *Streptomyces*, and *Staphylococcus*, although others may also be employed as a matter of choice.

As a representative but non-limiting example, useful expression vectors for bacterial use can comprise a selectable marker and bacterial origin of replication derived from commercially available plasmids comprising genetic elements of the well known cloning vector pBR322 (ATCC 37017). Such commercial vectors include, for example, pKK223-3 (Pharmacia Fine Chemicals, Uppsala, Sweden) and GEM 1 (Promega Biotech, Madison, WI, USA). These pBR322 "backbone" sections are combined with an appropriate promoter and the structural sequence to be expressed. Following transformation of a suitable host strain and growth of the host strain to an appropriate cell density, the selected promoter is induced or derepressed by appropriate means (*e.g.*, temperature shift or chemical induction) and cells are cultured for an additional period. Cells are typically harvested by centrifugation, disrupted by physical or chemical means, and the resulting crude extract retained for further purification.

Polynucleotides of the invention can also be used to induce immune responses. For example, as described in Fan et al., *Nat. Biotech.* 17:870-872 (1999), incorporated herein by reference, nucleic acid sequences encoding a polypeptide may be used to generate antibodies against the encoded polypeptide following topical administration of naked plasmid DNA or following injection, and preferably intramuscular injection of the DNA. The nucleic acid sequences are preferably inserted in a recombinant expression vector and may be in the form of naked DNA.

4.3 ANTISENSE

Another aspect of the invention pertains to isolated antisense nucleic acid molecules that are hybridizable to or complementary to the nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 1-30368, or fragments, analogs or derivatives thereof. An "antisense" nucleic acid comprises a nucleotide sequence that is complementary to a "sense" nucleic acid encoding a protein, *e.g.*, complementary to the coding strand of a double-stranded cDNA molecule or complementary to an mRNA sequence. In specific aspects, antisense nucleic acid molecules are provided that comprise a sequence complementary to at least about 10, 25, 50, 100, 250 or 500 nucleotides or an entire coding strand, or to only a portion thereof. Nucleic acid molecules encoding fragments, homologs, derivatives and analogs of a protein of any of SEQ ID

NO: 30369-60736 or antisense nucleic acids complementary to a nucleic acid sequence of SEQ ID NO: 1-30368 are additionally provided.

In one embodiment, an antisense nucleic acid molecule is antisense to a "coding region" of the coding strand of a nucleotide sequence of the invention. The term "coding region" refers to the region of the nucleotide sequence comprising codons which are translated into amino acid residues. In another embodiment, the antisense nucleic acid molecule is antisense to a "noncoding region" of the coding strand of a nucleotide sequence of the invention. The term "noncoding region" refers to 5' and 3' sequences which flank the coding region that are not translated into amino acids (*i.e.*, also referred to as 5' and 3' untranslated regions).

Given the coding strand sequences encoding a nucleic acid disclosed herein (*e.g.*, SEQ ID NO: 1-30368), antisense nucleic acids of the invention can be designed according to the rules of Watson and Crick or Hoogsteen base pairing. The antisense nucleic acid molecule can be complementary to the entire coding region of a mRNA, but more preferably is an oligonucleotide that is antisense to only a portion of the coding or noncoding region of a mRNA. For example, the antisense oligonucleotide can be complementary to the region surrounding the translation start site of a mRNA. An antisense oligonucleotide can be, for example, about 5, 10, 15, 20, 25, 30, 35, 40, 45 or 50 nucleotides in length. An antisense nucleic acid of the invention can be constructed using chemical synthesis or enzymatic ligation reactions using procedures known in the art. For example, an antisense nucleic acid (*e.g.*, an antisense oligonucleotide) can be chemically synthesized using naturally occurring nucleotides or variously modified nucleotides designed to increase the biological stability of the molecules or to increase the physical stability of the duplex formed between the antisense and sense nucleic acids, *e.g.*, phosphorothioate derivatives and acridine substituted nucleotides can be used.

Examples of modified nucleotides that can be used to generate the antisense nucleic acid include: 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xanthine, 4-acetylcytosine, 5-(carboxyhydroxylmethyl) uracil, 5-carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluracil, dihydrouracil, beta-D-galactosylqueosine, inosine, N6-isopentenyladenine, 1-methylguanine, 1-methylinosine, 2,2-dimethylguanine, 2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N6-adenine, 7-methylguanine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil, beta-D-mannosylqueosine, 5'-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methylthio-N6-isopentenyladenine, uracil-5-oxyacetic acid (v), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5-oxyacetic acid methylester, uracil-5-oxyacetic acid (v), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil, (acp3)w, and 2,6-diaminopurine. Alternatively, the

antisense nucleic acid can be produced biologically using an expression vector into which a nucleic acid has been subcloned in an antisense orientation (*i.e.*, RNA transcribed from the inserted nucleic acid will be of an antisense orientation to a target nucleic acid of interest, described further in the following subsection).

The antisense nucleic acid molecules of the invention are typically administered to a subject or generated *in situ* such that they hybridize with or bind to cellular mRNA and/or genomic DNA encoding a protein according to the invention to thereby inhibit expression of the protein, *e.g.*, by inhibiting transcription and/or translation. The hybridization can be by conventional nucleotide complementarity to form a stable duplex, or, for example, in the case of an antisense nucleic acid molecule that binds to DNA duplexes, through specific interactions in the major groove of the double helix. An example of a route of administration of antisense nucleic acid molecules of the invention includes direct injection at a tissue site. Alternatively, antisense nucleic acid molecules can be modified to target selected cells and then administered systemically. For example, for systemic administration, antisense molecules can be modified such that they specifically bind to receptors or antigens expressed on a selected cell surface, *e.g.*, by linking the antisense nucleic acid molecules to peptides or antibodies that bind to cell surface receptors or antigens. The antisense nucleic acid molecules can also be delivered to cells using the vectors described herein. To achieve sufficient intracellular concentrations of antisense molecules, vector constructs in which the antisense nucleic acid molecule is placed under the control of a strong pol II or pol III promoter are preferred.

In yet another embodiment, the antisense nucleic acid molecule of the invention is an -a n omeric nucleic acid molecule. An -a nomeric nucleic acid molecule forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual -uni ts, the strands run parallel to each other (Gaultier *et al.* (1987) *Nucleic Acids Res* 15: 6625-6641). The antisense nucleic acid molecule can also comprise a 2'-o-methylribonucleotide (Inoue *et al.* (1987) *Nucleic Acids Res* 15: 6131-6148) or a chimeric RNA -DNA analogue (Inoue *et al.* (1987) *FEBS Lett* 215: 327-330).

4.4 RIBOZYMES AND PNA MOIETIES

In still another embodiment, an antisense nucleic acid of the invention is a ribozyme. Ribozymes are catalytic RNA molecules with ribonuclease activity that are capable of cleaving a single-stranded nucleic acid, such as a mRNA, to which they have a complementary region. Thus, ribozymes (*e.g.*, hammerhead ribozymes (described in Haselhoff and Gerlach (1988) *Nature* 334:585-591)) can be used to catalytically cleave a mRNA transcripts to thereby inhibit translation of a mRNA. A ribozyme having specificity for a nucleic acid of the invention can be

designed based upon the nucleotide sequence of a DNA disclosed herein (*i.e.*, SEQ ID NO: 1-30368). For example, a derivative of a Tetrahymena L-19 IVS RNA can be constructed in which the nucleotide sequence of the active site is complementary to the nucleotide sequence to be cleaved in an mRNA of SEQ ID NO: 1-30368 (see, *e.g.*, Cech *et al.* U.S. Pat. No. 4,987,071; and Cech *et al.* U.S. Pat. No. 5,116,742). Alternatively, polynucleotides of the invention can be used to select a catalytic RNA having a specific ribonuclease activity from a pool of RNA molecules. See, *e.g.*, Bartel *et al.*, (1993) *Science* 261:1411-1418.

Alternatively, gene expression can be inhibited by targeting nucleotide sequences complementary to the regulatory region (*e.g.*, promoter and/or enhancers) to form triple helical structures that prevent transcription of the gene in target cells. See generally, Helene. (1991) *Anticancer Drug Des.* 6: 569-84; Helene. *et al.* (1992) *Ann. N.Y. Acad. Sci.* 660:27-36; and Maher (1992) *Bioassays* 14: 807-15.

In various embodiments, the nucleic acids of the invention can be modified at the base moiety, sugar moiety or phosphate backbone to improve, *e.g.*, the stability, hybridization, or solubility of the molecule. For example, the deoxyribose phosphate backbone of the nucleic acids can be modified to generate peptide nucleic acids (see Hyrup *et al.* (1996) *Bioorg Med Chem* 4: 5-23). As used herein, the terms "peptide nucleic acids" or "PNAs" refer to nucleic acid mimics, *e.g.*, DNA mimics, in which the deoxyribose phosphate backbone is replaced by a pseudopeptide backbone and only the four natural nucleobases are retained. The neutral backbone of PNAs has been shown to allow for specific hybridization to DNA and RNA under conditions of low ionic strength. The synthesis of PNA oligomers can be performed using standard solid phase peptide synthesis protocols as described in Hyrup *et al.* (1996) above; Perry-O'Keefe *et al.* (1996) *PNAS* 93: 14670-675.

PNAs of the invention can be used in therapeutic and diagnostic applications. For example, PNAs can be used as antisense or antigene agents for sequence-specific modulation of gene expression by, *e.g.*, inducing transcription or translation arrest or inhibiting replication. PNAs of the invention can also be used, *e.g.*, in the analysis of single base pair mutations in a gene by, *e.g.*, PNA directed PCR clamping; as artificial restriction enzymes when used in combination with other enzymes, *e.g.*, S1 nucleases (Hyrup B. (1996) above); or as probes or primers for DNA sequence and hybridization (Hyrup *et al.* (1996), above; Perry-O'Keefe (1996), above).

In another embodiment, PNAs of the invention can be modified, *e.g.*, to enhance their stability or cellular uptake, by attaching lipophilic or other helper groups to PNA, by the formation of PNA-DNA chimeras, or by the use of liposomes or other techniques of drug delivery known in the art. For example, PNA-DNA chimeras can be generated that may

combine the advantageous properties of PNA and DNA. Such chimeras allow DNA recognition enzymes, *e.g.*, RNase H and DNA polymerases, to interact with the DNA portion while the PNA portion would provide high binding affinity and specificity. PNA-DNA chimeras can be linked using linkers of appropriate lengths selected in terms of base stacking, number of bonds between the nucleobases, and orientation (Hyrup (1996) above). The synthesis of PNA-DNA chimeras can be performed as described in Hyrup (1996) above and Finn *et al.* (1996) *Nucl Acids Res* 24: 3357-63. For example, a DNA chain can be synthesized on a solid support using standard phosphoramidite coupling chemistry, and modified nucleoside analogs, *e.g.*, 5'-(4-methoxytrityl)amino-5'-deoxy-thymidine phosphoramidite, can be used between the PNA and the 5' end of DNA (Mag *et al.* (1989) *Nucl Acid Res* 17: 5973-88). PNA monomers are then coupled in a stepwise manner to produce a chimeric molecule with a 5' PNA segment and a 3' DNA segment (Finn *et al.* (1996) above). Alternatively, chimeric molecules can be synthesized with a 5' DNA segment and a 3' PNA segment. See, Petersen *et al.* (1975) *Bioorg Med Chem Lett* 5: 1119-11124.

In other embodiments, the oligonucleotide may include other appended groups such as peptides (*e.g.*, for targeting host cell receptors *in vivo*), or agents facilitating transport across the cell membrane (see, *e.g.*, Letsinger *et al.*, 1989, *Proc. Natl. Acad. Sci. U.S.A.* 86:6553-6556; Lemaitre *et al.*, 1987, Proc. *Natl. Acad. Sci.* 84:648-652; PCT Publication No. W088/09810) or the blood-brain barrier (see, *e.g.*, PCT Publication No. W089/10134). In addition, oligonucleotides can be modified with hybridization triggered cleavage agents (See, *e.g.*, Krol *et al.*, 1988, *BioTechniques* 6:958-976) or intercalating agents (see, *e.g.*, Zon, 1988, *Pharm. Res.* 5:539-549). To this end, the oligonucleotide may be conjugated to another molecule, *e.g.*, a peptide, a hybridization triggered cross-linking agent, a transport agent, a hybridization-triggered cleavage agent, etc.

4.5 HOSTS

The present invention further provides host cells genetically engineered to contain the polynucleotides of the invention. For example, such host cells may contain nucleic acids of the invention introduced into the host cell using known transformation, transfection or infection methods. The present invention still further provides host cells genetically engineered to express the polynucleotides of the invention, wherein such polynucleotides are in operative association with a regulatory sequence heterologous to the host cell which drives expression of the polynucleotides in the cell.

Knowledge of nucleic acid sequences allows for modification of cells to permit, or increase, expression of endogenous polypeptide. Cells can be modified (*e.g.*, by homologous

recombination) to provide increased polypeptide expression by replacing, in whole or in part, the naturally occurring promoter with all or part of a heterologous promoter so that the cells express the polypeptide at higher levels. The heterologous promoter is inserted in such a manner that it is operatively linked to the encoding sequences. See, for example, PCT International Publication No. WO94/12650, PCT International Publication No. WO92/20808, and PCT International Publication No. WO91/09955. It is also contemplated that, in addition to heterologous promoter DNA, amplifiable marker DNA (*e.g.*, ada, dhfr, and the multifunctional CAD gene which encodes carbamyl phosphate synthase, aspartate transcarbamylase, and dihydroorotase) and/or intron DNA may be inserted along with the heterologous promoter DNA. If linked to the coding sequence, amplification of the marker DNA by standard selection methods results in co-amplification of the desired protein coding sequences in the cells.

The host cell can be a higher eukaryotic host cell, such as a mammalian cell, a lower eukaryotic host cell, such as a yeast cell, or the host cell can be a prokaryotic cell, such as a bacterial cell. Introduction of the recombinant construct into the host cell can be effected by calcium phosphate transfection, DEAE, dextran mediated transfection, or electroporation (Davis, L. et al., *Basic Methods in Molecular Biology* (1986)). The host cells containing one of the polynucleotides of the invention, can be used in conventional manners to produce the gene product encoded by the isolated fragment (in the case of an ORF) or can be used to produce a heterologous protein under the control of the EMF.

Any host/vector system can be used to express one or more of the ORFs of the present invention. These include, but are not limited to, eukaryotic hosts such as HeLa cells, Cv-1 cell, COS cells, 293 cells, and Sf9 cells, as well as prokaryotic host such as *E. coli* and *B. subtilis*. The most preferred cells are those which do not normally express the particular polypeptide or protein or which expresses the polypeptide or protein at low natural level. Mature proteins can be expressed in mammalian cells, yeast, bacteria, or other cells under the control of appropriate promoters. Cell-free translation systems can also be employed to produce such proteins using RNAs derived from the DNA constructs of the present invention. Appropriate cloning and expression vectors for use with prokaryotic and eukaryotic hosts are described by Sambrook, et al., in Molecular Cloning: A Laboratory Manual, Second Edition, Cold Spring Harbor, New York (1989), the disclosure of which is hereby incorporated by reference.

Various mammalian cell culture systems can also be employed to express recombinant protein. Examples of mammalian expression systems include the COS-7 lines of monkey kidney fibroblasts, described by Gluzman, Cell 23:175 (1981). Other cell lines capable of expressing a compatible vector are, for example, the C127, monkey COS cells, Chinese Hamster Ovary (CHO) cells, human kidney 293 cells, human epidermal A431 cells, human Colo205 cells, 3T3

cells, CV-1 cells, other transformed primate cell lines, normal diploid cells, cell strains derived from *in vitro* culture of primary tissue, primary explants, HeLa cells, mouse L cells, BHK, HL-60, U937, HaK or Jurkat cells. Mammalian expression vectors will comprise an origin of replication, a suitable promoter and also any necessary ribosome binding sites, polyadenylation site, splice donor and acceptor sites, transcriptional termination sequences, and 5′ flanking nontranscribed sequences. DNA sequences derived from the SV40 viral genome, for example, SV40 origin, early promoter, enhancer, splice, and polyadenylation sites may be used to provide the required nontranscribed genetic elements. Recombinant polypeptides and proteins produced in bacterial culture are usually isolated by initial extraction from cell pellets, followed by one or more salting-out, aqueous ion exchange or size exclusion chromatography steps. Protein refolding steps can be used, as necessary, in completing configuration of the mature protein. Finally, high performance liquid chromatography (HPLC) can be employed for final purification steps. Microbial cells employed in expression of proteins can be disrupted by any convenient method, including freeze-thaw cycling, sonication, mechanical disruption, or use of cell lysing agents.

Alternatively, it may be possible to produce the protein in lower eukaryotes such as yeast or insects or in prokaryotes such as bacteria. Potentially suitable yeast strains include *Saccharomyces cerevisiae*, *Schizosaccharomyces pombe*, *Kluyveromyces* strains, *Candida*, or any yeast strain capable of expressing heterologous proteins. Potentially suitable bacterial strains include *Escherichia coli, Bacillus subtilis, Salmonella typhimurium*, or any bacterial strain capable of expressing heterologous proteins. If the protein is made in yeast or bacteria, it may be necessary to modify the protein produced therein, for example by phosphorylation or glycosylation of the appropriate sites, in order to obtain the functional protein. Such covalent attachments may be accomplished using known chemical or enzymatic methods.

In another embodiment of the present invention, cells and tissues may be engineered to express an endogenous gene comprising the polynucleotides of the invention under the control of inducible regulatory elements, in which case the regulatory sequences of the endogenous gene may be replaced by homologous recombination. As described herein, gene targeting can be used to replace a gene's existing regulatory region with a regulatory sequence isolated from a different gene or a novel regulatory sequence synthesized by genetic engineering methods. Such regulatory sequences may be comprised of promoters, enhancers, scaffold-attachment regions, negative regulatory elements, transcriptional initiation sites, regulatory protein binding sites or combinations of said sequences. Alternatively, sequences which affect the structure or stability of the RNA or protein produced may be replaced, removed, added, or otherwise modified by targeting. These sequence include polyadenylation signals, mRNA stability elements, splice

sites, leader sequences for enhancing or modifying transport or secretion properties of the protein, or other sequences which alter or improve the function or stability of protein or RNA molecules.

The targeting event may be a simple insertion of the regulatory sequence, placing the gene under the control of the new regulatory sequence, *e.g.*, inserting a new promoter or enhancer or both upstream of a gene. Alternatively, the targeting event may be a simple deletion of a regulatory element, such as the deletion of a tissue-specific negative regulatory element. Alternatively, the targeting event may replace an existing element; for example, a tissue-specific enhancer can be replaced by an enhancer that has broader or different cell-type specificity than the naturally occurring elements. Here, the naturally occurring sequences are deleted and new sequences are added. In all cases, the identification of the targeting event may be facilitated by the use of one or more selectable marker genes that are contiguous with the targeting DNA, allowing for the selection of cells in which the exogenous DNA has integrated into the host cell genome. The identification of the targeting event may also be facilitated by the use of one or more marker genes exhibiting the property of negative selection, such that the negatively selectable marker is linked to the exogenous DNA, but configured such that the negatively selectable marker flanks the targeting sequence, and such that a correct homologous recombination event with sequences in the host cell genome does not result in the stable integration of the negatively selectable marker. Markers useful for this purpose include the Herpes Simplex Virus thymidine kinase (TK) gene or the bacterial xanthine-guanine phosphoribosyl-transferase (gpt) gene.

The gene targeting or gene activation techniques which can be used in accordance with this aspect of the invention are more particularly described in U.S. Patent No. 5,272,071 to Chappel; U.S. Patent No. 5,578,461 to Sherwin et al.; International Application No. PCT/US92/09627 (WO93/09222) by Selden et al.; and International Application No. PCT/US90/06436 (WO91/06667) by Skoultchi et al., each of which is incorporated by reference herein in its entirety.

4.6 POLYPEPTIDES OF THE INVENTION

The isolated polypeptides of the invention include, but are not limited to, a polypeptide comprising: the amino acid sequences set forth as any one of SEQ ID NO: 30369-60736 or an amino acid sequence encoded by any one of the nucleotide sequences SEQ ID NO: 1-30368 or the corresponding full length or mature protein. Polypeptides of the invention also include polypeptides preferably with biological or immunological activity that are encoded by: (a) a polynucleotide having any one of the nucleotide sequences set forth in SEQ ID NO: 1-30368 or

(b) polynucleotides encoding any one of the amino acid sequences set forth as SEQ ID NO: 30369-60736 or (c) polynucleotides that hybridize to the complement of the polynucleotides of either (a) or (b) under stringent hybridization conditions. The invention also provides biologically active or immunologically active variants of any of the amino acid sequences set forth as SEQ ID NO: 30369-60736 or the corresponding full length or mature protein; and "substantial equivalents" thereof (*e.g.*, with at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, 86%, 87%, 88%, 89%, at least about 90%, 91%, 92%, 93%, 94%, typically at least about 95%, 96%, 97%, more typically at least about 98%, or most typically at least about 99% amino acid identity) that retain biological activity. Polypeptides encoded by allelic variants may have a similar, increased, or decreased activity compared to polypeptides comprising SEQ ID NO: 30369-60736.

Fragments of the proteins of the present invention which are capable of exhibiting biological activity are also encompassed by the present invention. Fragments of the protein may be in linear form or they may be cyclized using known methods, for example, as described in H. U. Saragovi, et al., Bio/Technology 10, 773-778 (1992) and in R. S. McDowell, et al., J. Amer. Chem. Soc. 114, 9245-9253 (1992), both of which are incorporated herein by reference. Such fragments may be fused to carrier molecules such as immunoglobulins for many purposes, including increasing the valency of protein binding sites.

The present invention also provides both full-length and mature forms (for example, without a signal sequence or precursor sequence) of the disclosed proteins. The protein coding sequence is identified in the sequence listing by translation of the disclosed nucleotide sequences. The mature form of such protein may be obtained by expression of a full-length polynucleotide in a suitable mammalian cell or other host cell. The sequence of the mature form of the protein is also determinable from the amino acid sequence of the full-length form. Where proteins of the present invention are membrane bound, soluble forms of the proteins are also provided. In such forms, part or all of the regions causing the proteins to be membrane bound are deleted so that the proteins are fully secreted from the cell in which they are expressed.

Protein compositions of the present invention may further comprise an acceptable carrier, such as a hydrophilic, *e.g.*, pharmaceutically acceptable, carrier.

The present invention further provides isolated polypeptides encoded by the nucleic acid fragments of the present invention or by degenerate variants of the nucleic acid fragments of the present invention. By "degenerate variant" is intended nucleotide fragments which differ from a nucleic acid fragment of the present invention (*e.g.*, an ORF) by nucleotide sequence but, due to the degeneracy of the genetic code, encode an identical polypeptide sequence. Preferred nucleic acid fragments of the present invention are the ORFs that encode proteins.

A variety of methodologies known in the art can be utilized to obtain any one of the isolated polypeptides or proteins of the present invention. At the simplest level, the amino acid sequence can be synthesized using commercially available peptide synthesizers. The synthetically-constructed protein sequences, by virtue of sharing primary, secondary or tertiary structural and/or conformational characteristics with proteins may possess biological properties in common therewith, including protein activity. This technique is particularly useful in producing small peptides and fragments of larger polypeptides. Fragments are useful, for example, in generating antibodies against the native polypeptide. Thus, they may be employed as biologically active or immunological substitutes for natural, purified proteins in screening of therapeutic compounds and in immunological processes for the development of antibodies.

The polypeptides and proteins of the present invention can alternatively be purified from cells which have been altered to express the desired polypeptide or protein. As used herein, a cell is said to be altered to express a desired polypeptide or protein when the cell, through genetic manipulation, is made to produce a polypeptide or protein which it normally does not produce or which the cell normally produces at a lower level. One skilled in the art can readily adapt procedures for introducing and expressing either recombinant or synthetic sequences into eukaryotic or prokaryotic cells in order to generate a cell which produces one of the polypeptides or proteins of the present invention.

The invention also relates to methods for producing a polypeptide comprising growing a culture of host cells of the invention in a suitable culture medium, and purifying the protein from the cells or the culture in which the cells are grown. For example, the methods of the invention include a process for producing a polypeptide in which a host cell containing a suitable expression vector that includes a polynucleotide of the invention is cultured under conditions that allow expression of the encoded polypeptide. The polypeptide can be recovered from the culture, conveniently from the culture medium, or from a lysate prepared from the host cells and further purified. Preferred embodiments include those in which the protein produced by such process is a full length or mature form of the protein.

In an alternative method, the polypeptide or protein is purified from bacterial cells which naturally produce the polypeptide or protein. One skilled in the art can readily follow known methods for isolating polypeptides and proteins in order to obtain one of the isolated polypeptides or proteins of the present invention. These include, but are not limited to, immunochromatography, HPLC, size-exclusion chromatography, ion-exchange chromatography, and immuno-affinity chromatography. See, *e.g.*, Scopes, *Protein Purification: Principles and Practice*, Springer-Verlag (1994); Sambrook, et al., in Molecular Cloning: *A Laboratory Manual*; Ausubel et al., *Current Protocols in Molecular Biology*. Polypeptide fragments that

retain biological/immunological activity include fragments comprising greater than about 100 amino acids, or greater than about 200 amino acids, and fragments that encode specific protein domains.

The purified polypeptides can be used in *in vitro* binding assays which are well known in the art to identify molecules which bind to the polypeptides. These molecules include but are not limited to, for *e.g.*, small molecules, molecules from combinatorial libraries, antibodies or other proteins. The molecules identified in the binding assay are then tested for antagonist or agonist activity in *in vivo* tissue culture or animal models that are well known in the art. In brief, the molecules are titrated into a plurality of cell cultures or animals and then tested for either cell/animal death or prolonged survival of the animal/cells.

In addition, the peptides of the invention or molecules capable of binding to the peptides may be complexed with toxins, *e.g.*, ricin or cholera, or with other compounds that are toxic to cells. The toxin-binding molecule complex is then targeted to a tumor or other cell by the specificity of the binding molecule for SEQ ID NO: 30369-60736.

The protein of the invention may also be expressed as a product of transgenic animals, *e.g.*, as a component of the milk of transgenic cows, goats, pigs, or sheep which are characterized by somatic or germ cells containing a nucleotide sequence encoding the protein.

The proteins provided herein also include proteins characterized by amino acid sequences similar to those of purified proteins but into which modification are naturally provided or deliberately engineered. For example, modifications in the peptide or DNA sequence can be made by those skilled in the art using known techniques. Modifications of interest in the protein sequences may include the alteration, substitution, replacement, insertion or deletion of a selected amino acid residue in the coding sequence. For example, one or more of the cysteine residues may be deleted or replaced with another amino acid to alter the conformation of the molecule. Techniques for such alteration, substitution, replacement, insertion or deletion are well known to those skilled in the art (see, *e.g.*, U.S. Pat. No. 4,518,584). Preferably, such alteration, substitution, replacement, insertion or deletion retains the desired activity of the protein. Regions of the protein that are important for the protein function can be determined by various methods known in the art including the alanine-scanning method which involved systematic substitution of single or strings of amino acids with alanine, followed by testing the resulting alanine-containing variant for biological activity. This type of analysis determines the importance of the substituted amino acid(s) in biological activity. Regions of the protein that are important for protein function may be determined by the eMATRIX program.

Other fragments and derivatives of the sequences of proteins which would be expected to retain protein activity in whole or in part and are useful for screening or other immunological

methodologies may also be easily made by those skilled in the art given the disclosures herein. Such modifications are encompassed by the present invention.

The protein may also be produced by operably linking the isolated polynucleotide of the invention to suitable control sequences in one or more insect expression vectors, and employing an insect expression system. Materials and methods for baculovirus/insect cell expression systems are commercially available in kit form from, *e.g.*, Invitrogen, San Diego, Calif., U.S.A. (the MaxBat™ kit), and such methods are well known in the art, as described in Summers and Smith, Texas Agricultural Experiment Station Bulletin No. 1555 (1987), incorporated herein by reference. As used herein, an insect cell capable of expressing a polynucleotide of the present invention is "transformed."

The protein of the invention may be prepared by culturing transformed host cells under culture conditions suitable to express the recombinant protein. The resulting expressed protein may then be purified from such culture (*i.e.*, from culture medium or cell extracts) using known purification processes, such as gel filtration and ion exchange chromatography. The purification of the protein may also include an affinity column containing agents which will bind to the protein; one or more column steps over such affinity resins as concanavalin A-agarose, heparin-toyopearl™ or Cibacrom blue 3GA Sepharose™; one or more steps involving hydrophobic interaction chromatography using such resins as phenyl ether, butyl ether, or propyl ether; or immunoaffinity chromatography.

Alternatively, the protein of the invention may also be expressed in a form that will facilitate purification. For example, it may be expressed as a fusion protein, such as those of maltose binding protein (MBP), glutathione-S-transferase (GST) or thioredoxin (TRX), or as a His-tag. Kits for expression and purification of such fusion proteins are commercially available from New England BioLab (Beverly, Mass.), Pharmacia (Piscataway, N.J.) and Invitrogen, respectively. The protein can also be tagged with an epitope and subsequently purified by using a specific antibody directed to such epitope. One such epitope ("FLAG®") is commercially available from Kodak (New Haven, Conn.).

Finally, one or more reverse-phase high performance liquid chromatography (RP- HPLC) steps employing hydrophobic RP-HPLC media, *e.g.*, silica gel having pendant methyl or other aliphatic groups, can be employed to further purify the protein. Some or all of the foregoing purification steps, in various combinations, can also be employed to provide a substantially homogeneous isolated recombinant protein. The protein thus purified is substantially free of other mammalian proteins and is defined in accordance with the present invention as an "isolated protein."

The polypeptides of the invention include analogs (variants). This embraces fragments, as well as peptides in which one or more amino acids has been deleted, inserted, or substituted. Also, analogs of the polypeptides of the invention embrace fusions of the polypeptides or modifications of the polypeptides of the invention, wherein the polypeptide or analog is fused to another moiety or moieties, *e.g.*, targeting moiety or another therapeutic agent. Such analogs may exhibit improved properties such as activity and/or stability. Examples of moieties which may be fused to the polypeptide or an analog include, for example, targeting moieties which provide for the delivery of polypeptide to pancreatic cells, *e.g.*, antibodies to pancreatic cells, antibodies to immune cells such as T-cells, monocytes, dendritic cells, granulocytes, etc., as well as receptor and ligands expressed on pancreatic or immune cells. Other moieties which may be fused to the polypeptide include therapeutic agents which are used for treatment, for example, immunosuppressive drugs such as cyclosporin, SK506, azathioprine, CD3 antibodies and steroids. Also, polypeptides may be fused to immune modulators, and other cytokines such as alpha or beta interferon.

4.6.1 DETERMINING POLYPEPTIDE AND POLYNUCLEOTIDE IDENTITY AND SIMILARITY

Preferred identity and/or similarity are designed to give the largest match between the sequences tested. Methods to determine identity and similarity are codified in computer programs including, but are not limited to, the GCG program package, including GAP (Devereux, J., et al., Nucleic Acids Research 12(1):387 (1984); Genetics Computer Group, University of Wisconsin, Madison, WI), BLASTP, BLASTN, BLASTX, FASTA (Altschul, S.F. et al., J. Molec. Biol. 215:403-410 (1990), PSI-BLAST (Altschul S.F. et al., Nucleic Acids Res. vol. 25, pp. 3389-3402, herein incorporated by reference), eMatrix software (Wu et al., J. Comp. Biol., Vol. 6, pp. 219-235 (1999), herein incorporated by reference), eMotif software (Nevill-Manning et al, ISMB-97, Vol. 4, pp. 202-209, herein incorporated by reference), pFam software (Sonnhammer et al., Nucleic Acids Res., Vol. 26(1), pp. 320-322 (1998), herein incorporated by reference) and the Kyte-Doolittle hydrophobocity prediction algorithm (J. Mol Biol, 157, pp. 105-31 (1982), incorporated herein by reference). The BLAST programs are publicly available from the National Center for Biotechnology Information (NCBI) and other sources (BLAST Manual, Altschul, S., et al. NCB NLM NIH Bethesda, MD 20894; Altschul, S., et al., J. Mol. Biol. 215:403-410 (1990).

4.7 CHIMERIC AND FUSION PROTEINS

The invention also provides chimeric or fusion proteins. As used herein, a "chimeric protein" or "fusion protein" comprises a polypeptide of the invention operatively linked to

another polypeptide. Within a fusion protein the polypeptide according to the invention can correspond to all or a portion of a protein according to the invention. In one embodiment, a fusion protein comprises at least one biologically active portion of a protein according to the invention. In another embodiment, a fusion protein comprises at least two biologically active portions of a protein according to the invention. Within the fusion protein, the term "operatively linked" is intended to indicate that the polypeptide according to the invention and the other polypeptide are fused in-frame to each other. The polypeptide can be fused to the N-terminus or C-terminus.

For example, in one embodiment a fusion protein comprises a polypeptide according to the invention operably linked to the extracellular domain of a second protein.

In another embodiment, the fusion protein is a GST-fusion protein in which the polypeptide sequences of the invention are fused to the C-terminus of the GST (*i.e.*, glutathione S-transferase) sequences.

In another embodiment, the fusion protein is an immunoglobulin fusion protein in which the polypeptide sequences according to the invention comprises one or more domains are fused to sequences derived from a member of the immunoglobulin protein family. The immunoglobulin fusion proteins of the invention can be incorporated into pharmaceutical compositions and administered to a subject to inhibit an interaction between a ligand and a protein of the invention on the surface of a cell, to thereby suppress signal transduction *in vivo*. The immunoglobulin fusion proteins can be used to affect the bioavailability of a cognate ligand. Inhibition of the ligand/protein interaction may be useful therapeutically for both the treatment of proliferative and differentiative disorders, *e,g.*, cancer as well as modulating (*e.g.*, promoting or inhibiting) cell survival. Moreover, the immunoglobulin fusion proteins of the invention can be used as immunogens to produce antibodies in a subject, to purify ligands, and in screening assays to identify molecules that inhibit the interaction of a polypeptide of the invention with a ligand.

A chimeric or fusion protein of the invention can be produced by standard recombinant DNA techniques. For example, DNA fragments coding for the different polypeptide sequences are ligated together in-frame in accordance with conventional techniques, *e.g.*, by employing blunt-ended or stagger-ended termini for ligation, restriction enzyme digestion to provide for appropriate termini, filling-in of cohesive ends as appropriate, alkaline phosphatase treatment to avoid undesirable joining, and enzymatic ligation. In another embodiment, the fusion gene can be synthesized by conventional techniques including automated DNA synthesizers. Alternatively, PCR amplification of gene fragments can be carried out using anchor primers that give rise to complementary overhangs between two consecutive gene fragments that can subsequently be annealed and reamplified to generate a chimeric gene sequence (see, for

example, Ausubel et al. (eds.) CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, 1992). Moreover, many expression vectors are commercially available that already encode a fusion moiety (*e.g.*, a GST polypeptide). A nucleic acid encoding a polypeptide of the invention can be cloned into such an expression vector such that the fusion moiety is linked in-frame to the protein of the invention.

4.8 GENE THERAPY

Mutations in the polynucleotides of the invention gene may result in loss of normal function of the encoded protein. The invention thus provides gene therapy to restore normal activity of the polypeptides of the invention; or to treat disease states involving polypeptides of the invention. Delivery of a functional gene encoding polypeptides of the invention to appropriate cells is effected *ex vivo*, *in situ*, or *in vivo* by use of vectors, and more particularly viral vectors (*e.g.*, adenovirus, adeno-associated virus, or a retrovirus), or *ex vivo* by use of physical DNA transfer methods (*e.g.*, liposomes or chemical treatments). See, for example, Anderson, Nature, supplement to vol. 392, no. 6679, pp.25-20 (1998). For additional reviews of gene therapy technology see Friedmann, Science, 244: 1275-1281 (1989); Verma, Scientific American: 68-84 (1990); and Miller, Nature, 357: 455-460 (1992). Introduction of any one of the nucleotides of the present invention or a gene encoding the polypeptides of the present invention can also be accomplished with extrachromosomal substrates (transient expression) or artificial chromosomes (stable expression). Cells may also be cultured *ex vivo* in the presence of proteins of the present invention in order to proliferate or to produce a desired effect on or activity in such cells. Treated cells can then be introduced *in vivo* for therapeutic purposes. Alternatively, it is contemplated that in other human disease states, preventing the expression of or inhibiting the activity of polypeptides of the invention will be useful in treating the disease states. It is contemplated that antisense therapy or gene therapy could be applied to negatively regulate the expression of polypeptides of the invention.

Other methods inhibiting expression of a protein include the introduction of antisense molecules to the nucleic acids of the present invention, their complements, or their translated RNA sequences, by methods known in the art. Further, the polypeptides of the present invention can be inhibited by using targeted deletion methods, or the insertion of a negative regulatory element such as a silencer, which is tissue specific.

The present invention still further provides cells genetically engineered *in vivo* to express the polynucleotides of the invention, wherein such polynucleotides are in operative association with a regulatory sequence heterologous to the host cell which drives expression of the polynucleotides in

the cell. These methods can be used to increase or decrease the expression of the polynucleotides of the present invention.

Knowledge of DNA sequences provided by the invention allows for modification of cells to permit, increase, or decrease, expression of endogenous polypeptide. Cells can be modified (*e.g.*, by homologous recombination) to provide increased polypeptide expression by replacing, in whole or in part, the naturally occurring promoter with all or part of a heterologous promoter so that the cells express the protein at higher levels. The heterologous promoter is inserted in such a manner that it is operatively linked to the desired protein encoding sequences. See, for example, PCT International Publication No. WO 94/12650, PCT International Publication No. WO 92/20808, and PCT International Publication No. WO 91/09955. It is also contemplated that, in addition to heterologous promoter DNA, amplifiable marker DNA (*e.g.*, ada, dhfr, and the multifunctional CAD gene which encodes carbamyl phosphate synthase, aspartate transcarbamylase, and dihydroorotase) and/or intron DNA may be inserted along with the heterologous promoter DNA. If linked to the desired protein coding sequence, amplification of the marker DNA by standard selection methods results in co-amplification of the desired protein coding sequences in the cells.

In another embodiment of the present invention, cells and tissues may be engineered to express an endogenous gene comprising the polynucleotides of the invention under the control of inducible regulatory elements, in which case the regulatory sequences of the endogenous gene may be replaced by homologous recombination. As described herein, gene targeting can be used to replace a gene's existing regulatory region with a regulatory sequence isolated from a different gene or a novel regulatory sequence synthesized by genetic engineering methods. Such regulatory sequences may be comprised of promoters, enhancers, scaffold-attachment regions, negative regulatory elements, transcriptional initiation sites, regulatory protein binding sites or combinations of said sequences. Alternatively, sequences which affect the structure or stability of the RNA or protein produced may be replaced, removed, added, or otherwise modified by targeting. These sequences include polyadenylation signals, mRNA stability elements, splice sites, leader sequences for enhancing or modifying transport or secretion properties of the protein, or other sequences which alter or improve the function or stability of protein or RNA molecules.

The targeting event may be a simple insertion of the regulatory sequence, placing the gene under the control of the new regulatory sequence, *e.g.*, inserting a new promoter or enhancer or both upstream of a gene. Alternatively, the targeting event may be a simple deletion of a regulatory element, such as the deletion of a tissue-specific negative regulatory element. Alternatively, the targeting event may replace an existing element; for example, a tissue-specific enhancer can be replaced by an enhancer that has broader or different cell-type specificity than the naturally occurring elements. Here, the naturally occurring sequences are deleted and new sequences are

added. In all cases, the identification of the targeting event may be facilitated by the use of one or more selectable marker genes that are contiguous with the targeting DNA, allowing for the selection of cells in which the exogenous DNA has integrated into the cell genome. The identification of the targeting event may also be facilitated by the use of one or more marker genes exhibiting the property of negative selection, such that the negatively selectable marker is linked to the exogenous DNA, but configured such that the negatively selectable marker flanks the targeting sequence, and such that a correct homologous recombination event with sequences in the host cell genome does not result in the stable integration of the negatively selectable marker. Markers useful for this purpose include the Herpes Simplex Virus thymidine kinase (TK) gene or the bacterial xanthine-guanine phosphoribosyl-transferase (gpt) gene.

The gene targeting or gene activation techniques which can be used in accordance with this aspect of the invention are more particularly described in U.S. Patent No. 5,272,071 to Chappel; U.S. Patent No. 5,578,461 to Sherwin et al.; International Application No. PCT/US92/09627 (WO93/09222) by Selden et al.; and International Application No. PCT/US90/06436 (WO91/06667) by Skoultchi et al., each of which is incorporated by reference herein in its entirety.

4.9 TRANSGENIC ANIMALS

In preferred methods to determine biological functions of the polypeptides of the invention in vivo, one or more genes provided by the invention are either over expressed or inactivated in the germ line of animals using homologous recombination [Capecchi, Science 244:1288-1292 (1989)]. Animals in which the gene is over expressed, under the regulatory control of exogenous or endogenous promoter elements, are known as transgenic animals. Animals in which an endogenous gene has been inactivated by homologous recombination are referred to as "knockout" animals. Knockout animals, preferably non-human mammals, can be prepared as described in U.S. Patent No. 5,557,032, incorporated herein by reference. Transgenic animals are useful to determine the roles polypeptides of the invention play in biological processes, and preferably in disease states. Transgenic animals are useful as model systems to identify compounds that modulate lipid metabolism. Transgenic animals, preferably non-human mammals, are produced using methods as described in U.S. Patent No 5,489,743 and PCT Publication No. WO94/28122, incorporated herein by reference.

Transgenic animals can be prepared wherein all or part of a promoter of the polynucleotides of the invention is either activated or inactivated to alter the level of expression of the polypeptides of the invention. Inactivation can be carried out using homologous recombination methods described above. Activation can be achieved by supplementing or even replacing the homologous promoter to provide for increased protein expression. The

homologous promoter can be supplemented by insertion of one or more heterologous enhancer elements known to confer promoter activation in a particular tissue.

The polynucleotides of the present invention also make possible the development, through, *e.g.*, homologous recombination or knock out strategies, of animals that fail to express polypeptides of the invention or that express a variant polypeptide. Such animals are useful as models for studying the *in vivo* activities of polypeptide as well as for studying modulators of the polypeptides of the invention.

In preferred methods to determine biological functions of the polypeptides of the invention *in vivo*, one or more genes provided by the invention are either over expressed or inactivated in the germ line of animals using homologous recombination [Capecchi, Science 244:1288-1292 (1989)]. Animals in which the gene is over expressed, under the regulatory control of exogenous or endogenous promoter elements, are known as transgenic animals. Animals in which an endogenous gene has been inactivated by homologous recombination are referred to as "knockout" animals. Knockout animals, preferably non-human mammals, can be prepared as described in U.S. Patent No. 5,557,032, incorporated herein by reference. Transgenic animals are useful to determine the roles polypeptides of the invention play in biological processes, and preferably in disease states. Transgenic animals are useful as model systems to identify compounds that modulate lipid metabolism. Transgenic animals, preferably non-human mammals, are produced using methods as described in U.S. Patent No 5,489,743 and PCT Publication No. WO94/28122, incorporated herein by reference.

Transgenic animals can be prepared wherein all or part of the polynucleotides of the invention promoter is either activated or inactivated to alter the level of expression of the polypeptides of the invention. Inactivation can be carried out using homologous recombination methods described above. Activation can be achieved by supplementing or even replacing the homologous promoter to provide for increased protein expression. The homologous promoter can be supplemented by insertion of one or more heterologous enhancer elements known to confer promoter activation in a particular tissue.

4.10 USES AND BIOLOGICAL ACTIVITY

The polynucleotides and proteins of the present invention are expected to exhibit one or more of the uses or biological activities (including those associated with assays cited herein) identified herein. Uses or activities described for proteins of the present invention may be provided by administration or use of such proteins or of polynucleotides encoding such proteins (such as, for example, in gene therapies or vectors suitable for introduction of DNA). The mechanism underlying the particular condition or pathology will dictate whether the

polypeptides of the invention, the polynucleotides of the invention or modulators (activators or inhibitors) thereof would be beneficial to the subject in need of treatment. Thus, "therapeutic compositions of the invention" include compositions comprising isolated polynucleotides (including recombinant DNA molecules, cloned genes and degenerate variants thereof) or polypeptides of the invention (including full length protein, mature protein and truncations or domains thereof), or compounds and other substances that modulate the overall activity of the target gene products, either at the level of target gene/protein expression or target protein activity. Such modulators include polypeptides, analogs, (variants), including fragments and fusion proteins, antibodies and other binding proteins; chemical compounds that directly or indirectly activate or inhibit the polypeptides of the invention (identified, *e.g.*, via drug screening assays as described herein); antisense polynucleotides and polynucleotides suitable for triple helix formation; and in particular antibodies or other binding partners that specifically recognize one or more epitopes of the polypeptides of the invention.

The polypeptides of the present invention may likewise be involved in cellular activation or in one of the other physiological pathways described herein.

4.10.1 RESEARCH USES AND UTILITIES

The polynucleotides provided by the present invention can be used by the research community for various purposes. The polynucleotides can be used to express recombinant protein for analysis, characterization or therapeutic use; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in disease states); as molecular weight markers on gels; as chromosome markers or tags (when labeled) to identify chromosomes or to map related gene positions; to compare with endogenous DNA sequences in patients to identify potential genetic disorders; as probes to hybridize and thus discover novel, related DNA sequences; as a source of information to derive PCR primers for genetic fingerprinting; as a probe to "subtract-out" known sequences in the process of discovering other novel polynucleotides; for selecting and making oligomers for attachment to a "gene chip" or other support, including for examination of expression patterns; to raise anti-protein antibodies using DNA immunization techniques; and as an antigen to raise anti-DNA antibodies or elicit another immune response. Where the polynucleotide encodes a protein which binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the polynucleotide can also be used in interaction trap assays (such as, for example, that described in Gyuris et al., Cell 75:791-803 (1993)) to identify polynucleotides encoding the other protein with which binding occurs or to identify inhibitors of the binding interaction.

The polypeptides provided by the present invention can similarly be used in assays to determine biological activity, including in a panel of multiple proteins for high-throughput screening; to raise antibodies or to elicit another immune response; as a reagent (including the labeled reagent) in assays designed to quantitatively determine levels of the protein (or its receptor) in biological fluids; as markers for tissues in which the corresponding polypeptide is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in a disease state); and, of course, to isolate correlative receptors or ligands. Proteins involved in these binding interactions can also be used to screen for peptide or small molecule inhibitors or agonists of the binding interaction.

Any or all of these research utilities are capable of being developed into reagent grade or kit format for commercialization as research products.

Methods for performing the uses listed above are well known to those skilled in the art. References disclosing such methods include without limitation "Molecular Cloning: A Laboratory Manual", 2d ed., Cold Spring Harbor Laboratory Press, Sambrook, J., E. F. Fritsch and T. Maniatis eds., 1989, and "Methods in Enzymology: Guide to Molecular Cloning Techniques", Academic Press, Berger, S. L. and A. R. Kimmel eds., 1987.

4.10.2 NUTRITIONAL USES

Polynucleotides and polypeptides of the present invention can also be used as nutritional sources or supplements. Such uses include without limitation use as a protein or amino acid supplement, use as a carbon source, use as a nitrogen source and use as a source of carbohydrate. In such cases the polypeptide or polynucleotide of the invention can be added to the feed of a particular organism or can be administered as a separate solid or liquid preparation, such as in the form of powder, pills, solutions, suspensions or capsules. In the case of microorganisms, the polypeptide or polynucleotide of the invention can be added to the medium in or on which the microorganism is cultured.

4.10.3 CYTOKINE AND CELL PROLIFERATION/DIFFERENTIATION ACTIVITY

A polypeptide of the present invention may exhibit activity relating to cytokine, cell proliferation (either inducing or inhibiting) or cell differentiation (either inducing or inhibiting) activity or may induce production of other cytokines in certain cell populations. A polynucleotide of the invention can encode a polypeptide exhibiting such attributes. Many protein factors discovered to date, including all known cytokines, have exhibited activity in one or more factor-dependent cell proliferation assays, and hence the assays serve as a convenient

confirmation of cytokine activity. The activity of therapeutic compositions of the present invention is evidenced by any one of a number of routine factor dependent cell proliferation assays for cell lines including, without limitation, 32D, DA2, DA1G, T10, B9, B9/11, BaF3, MC9/G, M+(preB M+), 2E8, RB5, DA1, 123, T1165, HT2, CTLL2, TF-1, Mo7e, CMK, HUVEC, and Caco. Therapeutic compositions of the invention can be used in the following:

Assays for T-cell or thymocyte proliferation include without limitation those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A. M. Kruisbeek, D. H. Margulies, E. M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, *In Vitro* assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Bertagnolli et al., J. Immunol. 145:1706-1712, 1990; Bertagnolli et al., Cellular Immunology 133:327-341, 1991; Bertagnolli, et al., I. Immunol. 149:3778-3783, 1992; Bowman et al., I. Immunol. 152:1756-1761, 1994.

Assays for cytokine production and/or proliferation of spleen cells, lymph node cells or thymocytes include, without limitation, those described in: Polyclonal T cell stimulation, Kruisbeek, A. M. and Shevach, E. M. In Current Protocols in Immunology. J. E. e.a. Coligan eds. Vol 1 pp. 3.12.1-3.12.14, John Wiley and Sons, Toronto. 1994; and Measurement of mouse and human interleukin-γ, Schreiber, R. D. In Current Protocols in Immunology. J. E. e.a. Coligan eds. Vol 1 pp. 6.8.1-6.8.8, John Wiley and Sons, Toronto. 1994.

Assays for proliferation and differentiation of hematopoietic and lymphopoietic cells include, without limitation, those described in: Measurement of Human and Murine Interleukin 2 and Interleukin 4, Bottomly, K., Davis, L. S. and Lipsky, P. E. In Current Protocols in Immunology. J. E. e.a. Coligan eds. Vol 1 pp. 6.3.1-6.3.12, John Wiley and Sons, Toronto. 1991; deVries et al., J. Exp. Med. 173:1205-1211, 1991; Moreau et al., Nature 336:690-692, 1988; Greenberger et al., Proc. Natl. Acad. Sci. U.S.A. 80:2931-2938, 1983; Measurement of mouse and human interleukin 6--Nordan, R. In Current Protocols in Immunology. J. E. Coligan eds. Vol 1 pp. 6.6.1-6.6.5, John Wiley and Sons, Toronto. 1991; Smith et al., Proc. Natl. Aced. Sci. U.S.A. 83:1857-1861, 1986; Measurement of human Interleukin 11--Bennett, F., Giannotti, J., Clark, S. C. and Turner, K. J. In Current Protocols in Immunology. J. E. Coligan eds. Vol 1 pp. 6.15.1 John Wiley and Sons, Toronto. 1991; Measurement of mouse and human Interleukin 9--Ciarletta, A., Giannotti, J., Clark, S. C. and Turner, K. J. In Current Protocols in Immunology. J. E. Coligan eds. Vol 1 pp. 6.13.1, John Wiley and Sons, Toronto. 1991.

Assays for T-cell clone responses to antigens (which will identify, among others, proteins that affect APC-T cell interactions as well as direct T-cell effects by measuring proliferation and cytokine production) include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A. M. Kruisbeek, D. H. Margulies, E. M. Shevach, W Strober,

Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, *In Vitro* assays for Mouse Lymphocyte Function; Chapter 6, Cytokines and their cellular receptors; Chapter 7, Immunologic studies in Humans); Weinberger et al., Proc. Natl. Acad. Sci. USA 77:6091-6095, 1980; Weinberger et al., Eur. J. Immun. 11:405-411, 1981; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988.

4.10.4 STEM CELL GROWTH FACTOR ACTIVITY

A polypeptide of the present invention may exhibit stem cell growth factor activity and be involved in the proliferation, differentiation and survival of pluripotent and totipotent stem cells including primordial germ cells, embryonic stem cells, hematopoietic stem cells and/or germ line stem cells. Administration of the polypeptide of the invention to stem cells *in vivo* or *ex vivo* is expected to maintain and expand cell populations in a totipotential or pluripotential state which would be useful for re-engineering damaged or diseased tissues, transplantation, manufacture of bio-pharmaceuticals and the development of bio-sensors. The ability to produce large quantities of human cells has important working applications for the production of human proteins which currently must be obtained from non-human sources or donors, implantation of cells to treat diseases such as Parkinson's, Alzheimer's and other neurodegenerative diseases; tissues for grafting such as bone marrow, skin, cartilage, tendons, bone, muscle (including cardiac muscle), blood vessels, cornea, neural cells, gastrointestinal cells and others; and organs for transplantation such as kidney, liver, pancreas (including islet cells), heart and lung.

It is contemplated that multiple different exogenous growth factors and/or cytokines may be administered in combination with the polypeptide of the invention to achieve the desired effect, including any of the growth factors listed herein, other stem cell maintenance factors, and specifically including stem cell factor (SCF), leukemia inhibitory factor (LIF), Flt-3 ligand (Flt-3L), any of the interleukins, recombinant soluble IL-6 receptor fused to IL-6, macrophage inflammatory protein 1-alpha (MIP-1-alpha), G-CSF, GM-CSF, thrombopoietin (TPO), platelet factor 4 (PF-4), platelet-derived growth factor (PDGF), neural growth factors and basic fibroblast growth factor (bFGF).

Since totipotent stem cells can give rise to virtually any mature cell type, expansion of these cells in culture will facilitate the production of large quantities of mature cells. Techniques for culturing stem cells are known in the art and administration of polypeptides of the invention, optionally with other growth factors and/or cytokines, is expected to enhance the survival and proliferation of the stem cell populations. This can be accomplished by direct administration of the polypeptide of the invention to the culture medium. Alternatively, stroma cells transfected with a polynucleotide that encodes for the polypeptide of the invention can be used as a feeder

layer for the stem cell populations in culture or in vivo. Stromal support cells for feeder layers may include embryonic bone marrow fibroblasts, bone marrow stromal cells, fetal liver cells, or cultured embryonic fibroblasts (see U.S. Patent No. 5,690,926).

Stem cells themselves can be transfected with a polynucleotide of the invention to induce autocrine expression of the polypeptide of the invention. This will allow for generation of undifferentiated totipotential/pluripotential stem cell lines that are useful as is or that can then be differentiated into the desired mature cell types. These stable cell lines can also serve as a source of undifferentiated totipotential/pluripotential mRNA to create cDNA libraries and templates for polymerase chain reaction experiments. These studies would allow for the isolation and identification of differentially expressed genes in stem cell populations that regulate stem cell proliferation and/or maintenance.

Expansion and maintenance of totipotent stem cell populations will be useful in the treatment of many pathological conditions. For example, polypeptides of the present invention may be used to manipulate stem cells in culture to give rise to neuroepithelial cells that can be used to augment or replace cells damaged by illness, autoimmune disease, accidental damage or genetic disorders. The polypeptide of the invention may be useful for inducing the proliferation of neural cells and for the regeneration of nerve and brain tissue, *i.e.* for the treatment of central and peripheral nervous system diseases and neuropathies, as well as mechanical and traumatic disorders which involve degeneration, death or trauma to neural cells or nerve tissue. In addition, the expanded stem cell populations can also be genetically altered for gene therapy purposes and to decrease host rejection of replacement tissues after grafting or implantation.

Expression of the polypeptide of the invention and its effect on stem cells can also be manipulated to achieve controlled differentiation of the stem cells into more differentiated cell types. A broadly applicable method of obtaining pure populations of a specific differentiated cell type from undifferentiated stem cell populations involves the use of a cell-type specific promoter driving a selectable marker. The selectable marker allows only cells of the desired type to survive. For example, stem cells can be induced to differentiate into cardiomyocytes (Wobus et al., Differentiation, 48: 173-182, (1991); Klug et al., J. Clin. Invest., 98(1): 216-224, (1998)) or skeletal muscle cells (Browder, L. W. In: *Principles of Tissue Engineering eds.* Lanza et al., Academic Press (1997)). Alternatively, directed differentiation of stem cells can be accomplished by culturing the stem cells in the presence of a differentiation factor such as retinoic acid and an antagonist of the polypeptide of the invention which would inhibit the effects of endogenous stem cell factor activity and allow differentiation to proceed.

In vitro cultures of stem cells can be used to determine if the polypeptide of the invention exhibits stem cell growth factor activity. Stem cells are isolated from any one of various cell

sources (including hematopoietic stem cells and embryonic stem cells) and cultured on a feeder layer, as described by Thompson et al. Proc. Natl. Acad. Sci, U.S.A., 92: 7844-7848 (1995), in the presence of the polypeptide of the invention alone or in combination with other growth factors or cytokines. The ability of the polypeptide of the invention to induce stem cells proliferation is determined by colony formation on semi-solid support *e.g.* as described by Bernstein et al., Blood, 77: 2316-2321 (1991).

4.10.5 HEMATOPOIESIS REGULATING ACTIVITY

A polypeptide of the present invention may be involved in regulation of hematopoiesis and, consequently, in the treatment of myeloid or lymphoid cell disorders. Even marginal biological activity in support of colony forming cells or of factor-dependent cell lines indicates involvement in regulating hematopoiesis, *e.g.* in supporting the growth and proliferation of erythroid progenitor cells alone or in combination with other cytokines, thereby indicating utility, for example, in treating various anemias or for use in conjunction with irradiation/chemotherapy to stimulate the production of erythroid precursors and/or erythroid cells; in supporting the growth and proliferation of myeloid cells such as granulocytes and monocytes/macrophages (*i.e.*, traditional CSF activity) useful, for example, in conjunction with chemotherapy to prevent or treat consequent myelo-suppression; in supporting the growth and proliferation of megakaryocytes and consequently of platelets thereby allowing prevention or treatment of various platelet disorders such as thrombocytopenia, and generally for use in place of or complimentary to platelet transfusions; and/or in supporting the growth and proliferation of hematopoietic stem cells which are capable of maturing to any and all of the above-mentioned hematopoietic cells and therefore find therapeutic utility in various stem cell disorders (such as those usually treated with transplantation, including, without limitation, aplastic anemia and paroxysmal nocturnal hemoglobinuria), as well as in repopulating the stem cell compartment post irradiation/chemotherapy, either *in-vivo* or *ex-vivo* (*i.e.*, in conjunction with bone marrow transplantation or with peripheral progenitor cell transplantation (homologous or heterologous)) as normal cells or genetically manipulated for gene therapy.

Therapeutic compositions of the invention can be used in the following:

Suitable assays for proliferation and differentiation of various hematopoietic lines are cited above.

Assays for embryonic stem cell differentiation (which will identify, among others, proteins that influence embryonic differentiation hematopoiesis) include, without limitation, those described in: Johansson et al. Cellular Biology 15:141-151, 1995; Keller et al., Molecular and Cellular Biology 13:473-486, 1993; McClanahan et al., Blood 81:2903-2915, 1993.

Assays for stem cell survival and differentiation (which will identify, among others, proteins that regulate lympho-hematopoiesis) include, without limitation, those described in: Methylcellulose colony forming assays, Freshney, M. G. In Culture of Hematopoietic Cells. R. I. Freshney, et al. eds. Vol pp. 265-268, Wiley-Liss, Inc., New York, N.Y. 1994; Hirayama et al., Proc. Natl. Acad. Sci. USA 89:5907-5911, 1992; Primitive hematopoietic colony forming cells with high proliferative potential, McNiece, I. K. and Briddell, R. A. In Culture of Hematopoietic Cells. R. I. Freshney, et al. eds. Vol pp. 23-39, Wiley-Liss, Inc., New York, N.Y. 1994; Neben et al., Experimental Hematology 22:353-359, 1994; Cobblestone area forming cell assay, Ploemacher, R. E. In Culture of Hematopoietic Cells. R. I. Freshney, et al. eds. Vol pp. 1-21, Wiley-Liss, Inc., New York, N.Y. 1994; Long term bone marrow cultures in the presence of stromal cells, Spooncer, E., Dexter, M. and Allen, T. In Culture of Hematopoietic Cells. R. I. Freshney, et al. eds. Vol pp. 163-179, Wiley-Liss, Inc., New York, N.Y. 1994; Long term culture initiating cell assay, Sutherland, H. J. In Culture of Hematopoietic Cells. R. I. Freshney, et al. eds. Vol pp. 139-162, Wiley-Liss, Inc., New York, N.Y. 1994.

4.10.6 TISSUE GROWTH ACTIVITY

A polypeptide of the present invention also may be involved in bone, cartilage, tendon, ligament and/or nerve tissue growth or regeneration, as well as in wound healing and tissue repair and replacement, and in healing of burns, incisions and ulcers.

A polypeptide of the present invention which induces cartilage and/or bone growth in circumstances where bone is not normally formed, has application in the healing of bone fractures and cartilage damage or defects in humans and other animals. Compositions of a polypeptide, antibody, binding partner, or other modulator of the invention may have prophylactic use in closed as well as open fracture reduction and also in the improved fixation of artificial joints. De novo bone formation induced by an osteogenic agent contributes to the repair of congenital, trauma induced, or oncologic resection induced craniofacial defects, and also is useful in cosmetic plastic surgery.

A polypeptide of this invention may also be involved in attracting bone-forming cells, stimulating growth of bone-forming cells, or inducing differentiation of progenitors of bone-forming cells. Treatment of osteoporosis, osteoarthritis, bone degenerative disorders, or periodontal disease, such as through stimulation of bone and/or cartilage repair or by blocking inflammation or processes of tissue destruction (collagenase activity, osteoclast activity, etc.) mediated by inflammatory processes may also be possible using the composition of the invention.

Another category of tissue regeneration activity that may involve the polypeptide of the present invention is tendon/ligament formation. Induction of tendon/ligament-like tissue or other tissue formation in circumstances where such tissue is not normally formed, has application in the healing of tendon or ligament tears, deformities and other tendon or ligament defects in humans and other animals. Such a preparation employing a tendon/ligament-like tissue inducing protein may have prophylactic use in preventing damage to tendon or ligament tissue, as well as use in the improved fixation of tendon or ligament to bone or other tissues, and in repairing defects to tendon or ligament tissue. De novo tendon/ligament-like tissue formation induced by a composition of the present invention contributes to the repair of congenital, trauma induced, or other tendon or ligament defects of other origin, and is also useful in cosmetic plastic surgery for attachment or repair of tendons or ligaments. The compositions of the present invention may provide environment to attract tendon- or ligament-forming cells, stimulate growth of tendon- or ligament-forming cells, induce differentiation of progenitors of tendon- or ligament-forming cells, or induce growth of tendon/ligament cells or progenitors *ex vivo* for return *in vivo* to effect tissue repair. The compositions of the invention may also be useful in the treatment of tendinitis, carpal tunnel syndrome and other tendon or ligament defects. The compositions may also include an appropriate matrix and/or sequestering agent as a carrier as is well known in the art.

The compositions of the present invention may also be useful for proliferation of neural cells and for regeneration of nerve and brain tissue, *i.e.* for the treatment of central and peripheral nervous system diseases and neuropathies, as well as mechanical and traumatic disorders, which involve degeneration, death or trauma to neural cells or nerve tissue. More specifically, a composition may be used in the treatment of diseases of the peripheral nervous system, such as peripheral nerve injuries, peripheral neuropathy and localized neuropathies, and central nervous system diseases, such as Alzheimer's, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and Shy-Drager syndrome. Further conditions that may be treated in accordance with the present invention include mechanical and traumatic disorders, such as spinal cord disorders, head trauma and cerebrovascular diseases such as stroke. Peripheral neuropathies resulting from chemotherapy or other medical therapies may also be treatable using a composition of the invention.

Compositions of the invention may also be useful to promote better or faster closure of non-healing wounds, including without limitation pressure ulcers, ulcers associated with vascular insufficiency, surgical and traumatic wounds, and the like.

Compositions of the present invention may also be involved in the generation or regeneration of other tissues, such as organs (including, for example, pancreas, liver, intestine,

kidney, skin, endothelium), muscle (smooth, skeletal or cardiac) and vascular (including vascular endothelium) tissue, or for promoting the growth of cells comprising such tissues. Part of the desired effects may be by inhibition or modulation of fibrotic scarring may allow normal tissue to regenerate. A polypeptide of the present invention may also exhibit angiogenic activity.

A composition of the present invention may also be useful for gut protection or regeneration and treatment of lung or liver fibrosis, reperfusion injury in various tissues, and conditions resulting from systemic cytokine damage.

A composition of the present invention may also be useful for promoting or inhibiting differentiation of tissues described above from precursor tissues or cells; or for inhibiting the growth of tissues described above.

Therapeutic compositions of the invention can be used in the following:

Assays for tissue generation activity include, without limitation, those described in: International Patent Publication No. WO95/16035 (bone, cartilage, tendon); International Patent Publication No. WO95/05846 (nerve, neuronal); International Patent Publication No. WO91/07491 (skin, endothelium).

Assays for wound healing activity include, without limitation, those described in: Winter, Epidermal Wound Healing, pps. 71-112 (Maibach, H. I. and Rovee, D. T., eds.), Year Book Medical Publishers, Inc., Chicago, as modified by Eaglstein and Mertz, J. Invest. Dermatol 71:382-84 (1978).

4.10.7 IMMUNE STIMULATING OR SUPPRESSING ACTIVITY

A polypeptide of the present invention may also exhibit immune stimulating or immune suppressing activity, including without limitation the activities for which assays are described herein. A polynucleotide of the invention can encode a polypeptide exhibiting such activities. A protein may be useful in the treatment of various immune deficiencies and disorders (including severe combined immunodeficiency (SCID)), *e.g.*, in regulating (up or down) growth and proliferation of T and/or B lymphocytes, as well as effecting the cytolytic activity of NK cells and other cell populations. These immune deficiencies may be genetic or be caused by viral (*e.g.*, HIV) as well as bacterial or fungal infections, or may result from autoimmune disorders. More specifically, infectious diseases causes by viral, bacterial, fungal or other infection may be treatable using a protein of the present invention, including infections by HIV, hepatitis viruses, herpes viruses, mycobacteria, Leishmania spp., malaria spp. and various fungal infections such as candidiasis. Of course, in this regard, proteins of the present invention may also be useful where a boost to the immune system generally may be desirable, *i.e.*, in the treatment of cancer.

Autoimmune disorders which may be treated using a protein of the present invention include, for example, connective tissue disease, multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, autoimmune pulmonary inflammation, Guillain-Barre syndrome, autoimmune thyroiditis, insulin dependent diabetes mellitis, myasthenia gravis, graft-versus-host disease and autoimmune inflammatory eye disease. Such a protein (or antagonists thereof, including antibodies) of the present invention may also to be useful in the treatment of allergic reactions and conditions (*e.g.*, anaphylaxis, serum sickness, drug reactions, food allergies, insect venom allergies, mastocytosis, allergic rhinitis, hypersensitivity pneumonitis, urticaria, angioedema, eczema, atopic dermatitis, allergic contact dermatitis, erythema multiforme, Stevens-Johnson syndrome, allergic conjunctivitis, atopic keratoconjunctivitis, venereal keratoconjunctivitis, giant papillary conjunctivitis and contact allergies), such as asthma (particularly allergic asthma) or other respiratory problems. Other conditions, in which immune suppression is desired (including, for example, organ transplantation), may also be treatable using a protein (or antagonists thereof) of the present invention. The therapeutic effects of the polypeptides or antagonists thereof on allergic reactions can be evaluated by in vivo animals models such as the cumulative contact enhancement test (Lastbom et al., Toxicology 125: 59-66, 1998), skin prick test (Hoffmann et al., Allergy 54: 446-54, 1999), guinea pig skin sensitization test (Vohr et al., Arch. Toxocol. 73: 501-9), and murine local lymph node assay (Kimber et al., J. Toxicol. Environ. Health 53: 563-79).

Using the proteins of the invention it may also be possible to modulate immune responses, in a number of ways. Down regulation may be in the form of inhibiting or blocking an immune response already in progress or may involve preventing the induction of an immune response. The functions of activated T cells may be inhibited by suppressing T cell responses or by inducing specific tolerance in T cells, or both. Immunosuppression of T cell responses is generally an active, non-antigen-specific, process which requires continuous exposure of the T cells to the suppressive agent. Tolerance, which involves inducing non-responsiveness or anergy in T cells, is distinguishable from immunosuppression in that it is generally antigen-specific and persists after exposure to the tolerizing agent has ceased. Operationally, tolerance can be demonstrated by the lack of a T cell response upon reexposure to specific antigen in the absence of the tolerizing agent.

Down regulating or preventing one or more antigen functions (including without limitation B lymphocyte antigen functions (such as, for example, B7)), *e.g.*, preventing high level lymphokine synthesis by activated T cells, will be useful in situations of tissue, skin and organ transplantation and in graft-versus-host disease (GVHD). For example, blockage of T cell function should result in reduced tissue destruction in tissue transplantation. Typically, in tissue

transplants, rejection of the transplant is initiated through its recognition as foreign by T cells, followed by an immune reaction that destroys the transplant. The administration of a therapeutic composition of the invention may prevent cytokine synthesis by immune cells, such as T cells, and thus acts as an immunosuppressant. Moreover, a lack of costimulation may also be sufficient to anergize the T cells, thereby inducing tolerance in a subject. Induction of long-term tolerance by B lymphocyte antigen-blocking reagents may avoid the necessity of repeated administration of these blocking reagents. To achieve sufficient immunosuppression or tolerance in a subject, it may also be necessary to block the function of a combination of B lymphocyte antigens.

The efficacy of particular therapeutic compositions in preventing organ transplant rejection or GVHD can be assessed using animal models that are predictive of efficacy in humans. Examples of appropriate systems which can be used include allogeneic cardiac grafts in rats and xenogeneic pancreatic islet cell grafts in mice, both of which have been used to examine the immunosuppressive effects of CTLA4Ig fusion proteins in vivo as described in Lenschow et al., Science 257:789-792 (1992) and Turka et al., Proc. Natl. Acad. Sci USA, 89:11102-11105 (1992). In addition, murine models of GVHD (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 846-847) can be used to determine the effect of therapeutic compositions of the invention on the development of that disease.

Blocking antigen function may also be therapeutically useful for treating autoimmune diseases. Many autoimmune disorders are the result of inappropriate activation of T cells that are reactive against self-tissue and which promote the production of cytokines and autoantibodies involved in the pathology of the diseases. Preventing the activation of autoreactive T cells may reduce or eliminate disease symptoms. Administration of reagents which block stimulation of T cells can be used to inhibit T cell activation and prevent production of autoantibodies or T cell-derived cytokines which may be involved in the disease process. Additionally, blocking reagents may induce antigen-specific tolerance of autoreactive T cells which could lead to long-term relief from the disease. The efficacy of blocking reagents in preventing or alleviating autoimmune disorders can be determined using a number of well-characterized animal models of human autoimmune diseases. Examples include murine experimental autoimmune encephalitis, systemic lupus erythmatosis in MRL/lpr/lpr mice or NZB hybrid mice, murine autoimmune collagen arthritis, diabetes mellitus in NOD mice and BB rats, and murine experimental myasthenia gravis (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 840-856).

Upregulation of an antigen function (*e.g.*, a B lymphocyte antigen function), as a means of up regulating immune responses, may also be useful in therapy. Upregulation of immune

responses may be in the form of enhancing an existing immune response or eliciting an initial immune response. For example, enhancing an immune response may be useful in cases of viral infection, including systemic viral diseases such as influenza, the common cold, and encephalitis.

Alternatively, anti-viral immune responses may be enhanced in an infected patient by removing T cells from the patient, costimulating the T cells in vitro with viral antigen-pulsed APCs either expressing a peptide of the present invention or together with a stimulatory form of a soluble peptide of the present invention and reintroducing the in vitro activated T cells into the patient. Another method of enhancing anti-viral immune responses would be to isolate infected cells from a patient, transfect them with a nucleic acid encoding a protein of the present invention as described herein such that the cells express all or a portion of the protein on their surface, and reintroduce the transfected cells into the patient. The infected cells would now be capable of delivering a costimulatory signal to, and thereby activate, T cells in vivo.

A polypeptide of the present invention may provide the necessary stimulation signal to T cells to induce a T cell mediated immune response against the transfected tumor cells. In addition, tumor cells which lack MHC class I or MHC class II molecules, or which fail to reexpress sufficient mounts of MHC class I or MHC class II molecules, can be transfected with nucleic acid encoding all or a portion of (*e.g.*, a cytoplasmic-domain truncated portion) of an MHC class I alpha chain protein and β_2 microglobulin protein or an MHC class II alpha chain protein and an MHC class II beta chain protein to thereby express MHC class I or MHC class II proteins on the cell surface. Expression of the appropriate class I or class II MHC in conjunction with a peptide having the activity of a B lymphocyte antigen (*e.g.*, B7-1, B7-2, B7-3) induces a T cell mediated immune response against the transfected tumor cell. Optionally, a gene encoding an antisense construct which blocks expression of an MHC class II associated protein, such as the invariant chain, can also be cotransfected with a DNA encoding a peptide having the activity of a B lymphocyte antigen to promote presentation of tumor associated antigens and induce tumor specific immunity. Thus, the induction of a T cell mediated immune response in a human subject may be sufficient to overcome tumor-specific tolerance in the subject.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for thymocyte or splenocyte cytotoxicity include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A. M. Kruisbeek, D. H. Margulies, E. M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Herrmann et al., Proc. Natl. Acad. Sci. USA

78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., I. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Bowman et al., J. Virology 61:1992-1998; Bertagnolli et al., Cellular Immunology 133:327-341, 1991; Brown et al., J. Immunol. 153:3079-3092, 1994.

Assays for T-cell-dependent immunoglobulin responses and isotype switching (which will identify, among others, proteins that modulate T-cell dependent antibody responses and that affect Th1/Th2 profiles) include, without limitation, those described in: Maliszewski, J. Immunol. 144:3028-3033, 1990; and Assays for B cell function: In vitro antibody production, Mond, J. J. and Brunswick, M. In Current Protocols in Immunology. J. E. e.a. Coligan eds. Vol 1 pp. 3.8.1-3.8.16, John Wiley and Sons, Toronto. 1994.

Mixed lymphocyte reaction (MLR) assays (which will identify, among others, proteins that generate predominantly Th1 and CTL responses) include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A. M. Kruisbeek, D. H. Margulies, E. M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., J. Immunol. 149:3778-3783, 1992.

Dendritic cell-dependent assays (which will identify, among others, proteins expressed by dendritic cells that activate naive T-cells) include, without limitation, those described in: Guery et al., J. Immunol. 134:536-544, 1995; Inaba et al., Journal of Experimental Medicine 173:549-559, 1991; Macatonia et al., Journal of Immunology 154:5071-5079, 1995; Porgador et al., Journal of Experimental Medicine 182:255-260, 1995; Nair et al., Journal of Virology 67:4062-4069, 1993; Huang et al., Science 264:961-965, 1994; Macatonia et al., Journal of Experimental Medicine 169:1255-1264, 1989; Bhardwaj et al., Journal of Clinical Investigation 94:797-807, 1994; and Inaba et al., Journal of Experimental Medicine 172:631-640, 1990.

Assays for lymphocyte survival/apoptosis (which will identify, among others, proteins that prevent apoptosis after superantigen induction and proteins that regulate lymphocyte homeostasis) include, without limitation, those described in: Darzynkiewicz et al., Cytometry 13:795-808, 1992; Gorczyca et al., Leukemia 7:659-670, 1993; Gorczyca et al., Cancer Research 53:1945-1951, 1993; Itoh et al., Cell 66:233-243, 1991; Zacharchuk, Journal of Immunology 145:4037-4045, 1990; Zamai et al., Cytometry 14:891-897, 1993; Gorczyca et al., International Journal of Oncology 1:639-648, 1992.

Assays for proteins that influence early steps of T-cell commitment and development include, without limitation, those described in: Antica et al., Blood 84:111-117, 1994; Fine et

al., Cellular Immunology 155:111-122, 1994; Galy et al., Blood 85:2770-2778, 1995; Toki et al., Proc. Nat. Acad Sci. USA 88:7548-7551, 1991.

4.10.8 ACTIVIN/INHIBIN ACTIVITY

A polypeptide of the present invention may also exhibit activin- or inhibin-related activities. A polynucleotide of the invention may encode a polypeptide exhibiting such characteristics. Inhibins are characterized by their ability to inhibit the release of follicle stimulating hormone (FSH), while activins and are characterized by their ability to stimulate the release of follicle stimulating hormone (FSH). Thus, a polypeptide of the present invention, alone or in heterodimers with a member of the inhibin family, may be useful as a contraceptive based on the ability of inhibins to decrease fertility in female mammals and decrease spermatogenesis in male mammals. Administration of sufficient amounts of other inhibins can induce infertility in these mammals. Alternatively, the polypeptide of the invention, as a homodimer or as a heterodimer with other protein subunits of the inhibin group, may be useful as a fertility inducing therapeutic, based upon the ability of activin molecules in stimulating FSH release from cells of the anterior pituitary. See, for example, U.S. Pat. No. 4,798,885. A polypeptide of the invention may also be useful for advancement of the onset of fertility in sexually immature mammals, so as to increase the lifetime reproductive performance of domestic animals such as, but not limited to, cows, sheep and pigs.

The activity of a polypeptide of the invention may, among other means, be measured by the following methods.

Assays for activin/inhibin activity include, without limitation, those described in: Vale et al., Endocrinology 91:562-572, 1972; Ling et al., Nature 321:779-782, 1986; Vale et al., Nature 321:776-779, 1986; Mason et al., Nature 318:659-663, 1985; Forage et al., Proc. Natl. Acad. Sci. USA 83:3091-3095, 1986.

4.10.9 CHEMOTACTIC/CHEMOKINETIC ACTIVITY

A polypeptide of the present invention may be involved in chemotactic or chemokinetic activity for mammalian cells, including, for example, monocytes, fibroblasts, neutrophils, T-cells, mast cells, eosinophils, epithelial and/or endothelial cells. A polynucleotide of the invention can encode a polypeptide exhibiting such attributes. Chemotactic and chemokinetic receptor activation can be used to mobilize or attract a desired cell population to a desired site of action. Chemotactic or chemokinetic compositions (*e.g.* proteins, antibodies, binding partners, or modulators of the invention) provide particular advantages in treatment of wounds and other trauma to tissues, as well as in treatment of localized infections. For example, attraction of

lymphocytes, monocytes or neutrophils to tumors or sites of infection may result in improved immune responses against the tumor or infecting agent.

A protein or peptide has chemotactic activity for a particular cell population if it can stimulate, directly or indirectly, the directed orientation or movement of such cell population. Preferably, the protein or peptide has the ability to directly stimulate directed movement of cells. Whether a particular protein has chemotactic activity for a population of cells can be readily determined by employing such protein or peptide in any known assay for cell chemotaxis.

Therapeutic compositions of the invention can be used in the following:

Assays for chemotactic activity (which will identify proteins that induce or prevent chemotaxis) consist of assays that measure the ability of a protein to induce the migration of cells across a membrane as well as the ability of a protein to induce the adhesion of one cell population to another cell population. Suitable assays for movement and adhesion include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A. M. Kruisbeek, D. H. Marguiles, E. M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 6.12, Measurement of alpha and beta Chemokines 6.12.1-6.12.28; Taub et al. J. Clin. Invest. 95:1370-1376, 1995; Lind et al. APMIS 103:140-146, 1995; Muller et al Eur. J. Immunol. 25:1744-1748; Gruber et al. J. of Immunol. 152:5860-5867, 1994; Johnston et al. J. of Immunol. 153:1762-1768, 1994.

4.10.10 HEMOSTATIC AND THROMBOLYTIC ACTIVITY

A polypeptide of the invention may also be involved in hemostatis or thrombolysis or thrombosis. A polynucleotide of the invention can encode a polypeptide exhibiting such attributes. Compositions may be useful in treatment of various coagulation disorders (including hereditary disorders, such as hemophilias) or to enhance coagulation and other hemostatic events in treating wounds resulting from trauma, surgery or other causes. A composition of the invention may also be useful for dissolving or inhibiting formation of thromboses and for treatment and prevention of conditions resulting therefrom (such as, for example, infarction of cardiac and central nervous system vessels (*e.g.*, stroke).

Therapeutic compositions of the invention can be used in the following:

Assay for hemostatic and thrombolytic activity include, without limitation, those described in: Linet et al., J. Clin. Pharmacol. 26:131-140, 1986; Burdick et al., Thrombosis Res. 45:413-419, 1987; Humphrey et al., Fibrinolysis 5:71-79 (1991); Schaub, Prostaglandins 35:467-474, 1988.

4.10.11 CANCER DIAGNOSIS AND THERAPY

Polypeptides of the invention may be involved in cancer cell generation, proliferation or metastasis. Detection of the presence or amount of polynucleotides or polypeptides of the invention may be useful for the diagnosis and/or prognosis of one or more types of cancer. For example, the presence or increased expression of a polynucleotide/polypeptide of the invention may indicate a hereditary risk of cancer, a precancerous condition, or an ongoing malignancy. Conversely, a defect in the gene or absence of the polypeptide may be associated with a cancer condition. Identification of single nucleotide polymorphisms associated with cancer or a predisposition to cancer may also be useful for diagnosis or prognosis.

Cancer treatments promote tumor regression by inhibiting tumor cell proliferation, inhibiting angiogenesis (growth of new blood vessels that is necessary to support tumor growth) and/or prohibiting metastasis by reducing tumor cell motility or invasiveness. Therapeutic compositions of the invention may be effective in adult and pediatric oncology including in solid phase tumors/malignancies, locally advanced tumors, human soft tissue sarcomas, metastatic cancer, including lymphatic metastases, blood cell malignancies including multiple myeloma, acute and chronic leukemias, and lymphomas, head and neck cancers including mouth cancer, larynx cancer and thyroid cancer, lung cancers including small cell carcinoma and non-small cell cancers, breast cancers including small cell carcinoma and ductal carcinoma, gastrointestinal cancers including esophageal cancer, stomach cancer, colon cancer, colorectal cancer and polyps associated with colorectal neoplasia, pancreatic cancers, liver cancer, urologic cancers including bladder cancer and prostate cancer, malignancies of the female genital tract including ovarian carcinoma, uterine (including endometrial) cancers, and solid tumor in the ovarian follicle, kidney cancers including renal cell carcinoma, brain cancers including intrinsic brain tumors, neuroblastoma, astrocytic brain tumors, gliomas, metastatic tumor cell invasion in the central nervous system, bone cancers including osteomas, skin cancers including malignant melanoma, tumor progression of human skin keratinocytes, squamous cell carcinoma, basal cell carcinoma, hemangiopericytoma and Karposi's sarcoma.

Polypeptides, polynucleotides, or modulators of polypeptides of the invention (including inhibitors and stimulators of the biological activity of the polypeptide of the invention) may be administered to treat cancer. Therapeutic compositions can be administered in therapeutically effective dosages alone or in combination with adjuvant cancer therapy such as surgery, chemotherapy, radiotherapy, thermotherapy, and laser therapy, and may provide a beneficial effect, *e.g.* reducing tumor size, slowing rate of tumor growth, inhibiting metastasis, or otherwise improving overall clinical condition, without necessarily eradicating the cancer.

The composition can also be administered in therapeutically effective amounts as a portion of an anti-cancer cocktail. An anti-cancer cocktail is a mixture of the polypeptide or

modulator of the invention with one or more anti-cancer drugs in addition to a pharmaceutically acceptable carrier for delivery. The use of anti-cancer cocktails as a cancer treatment is routine. Anti-cancer drugs that are well known in the art and can be used as a treatment in combination with the polypeptide or modulator of the invention include: Actinomycin D, Aminoglutethimide, Asparaginase, Bleomycin, Busulfan, Carboplatin, Carmustine, Chlorambucil, Cisplatin (cis-DDP), Cyclophosphamide, Cytarabine HCl (Cytosine arabinoside), Dacarbazine, Dactinomycin, Daunorubicin HCl, Doxorubicin HCl, Estramustine phosphate sodium, Etoposide (V16-213), Floxuridine, 5-Fluorouracil (5-Fu), Flutamide, Hydroxyurea (hydroxycarbamide), Ifosfamide, Interferon Alpha-2a, Interferon Alpha-2b, Leuprolide acetate (LHRH-releasing factor analog), Lomustine, Mechlorethamine HCl (nitrogen mustard), Melphalan, Mercaptopurine, Mesna, Methotrexate (MTX), Mitomycin, Mitoxantrone HCl, Octreotide, Plicamycin, Procarbazine HCl, Streptozocin, Tamoxifen citrate, Thioguanine, Thiotepa, Vinblastine sulfate, Vincristine sulfate, Amsacrine, Azacitidine, Hexamethylmelamine, Interleukin-2, Mitoguazone, Pentostatin, Semustine, Teniposide, and Vindesine sulfate.

In addition, therapeutic compositions of the invention may be used for prophylactic treatment of cancer. There are hereditary conditions and/or environmental situations (*e.g.* exposure to carcinogens) known in the art that predispose an individual to developing cancers. Under these circumstances, it may be beneficial to treat these individuals with therapeutically effective doses of the polypeptide of the invention to reduce the risk of developing cancers.

In vitro models can be used to determine the effective doses of the polypeptide of the invention as a potential cancer treatment. These *in vitro* models include proliferation assays of cultured tumor cells, growth of cultured tumor cells in soft agar (see Freshney, (1987) Culture of Animal Cells: A Manual of Basic Technique, Wily-Liss, New York, NY Ch 18 and Ch 21), tumor systems in nude mice as described in Giovanella et al., J. Natl. Can. Inst., 52: 921-30 (1974), mobility and invasive potential of tumor cells in Boyden Chamber assays as described in Pilkington et al., Anticancer Res., 17: 4107-9 (1997), and angiogenesis assays such as induction of vascularization of the chick chorioallantoic membrane or induction of vascular endothelial cell migration as described in Ribatta et al., Intl. J. Dev. Biol., 40: 1189-97 (1999) and Li et al., Clin. Exp. Metastasis, 17:423-9 (1999), respectively. Suitable tumor cells lines are available, *e.g.* from American Type Tissue Culture Collection catalogs.

4.10.12 RECEPTOR/LIGAND ACTIVITY

A polypeptide of the present invention may also demonstrate activity as receptor, receptor ligand or inhibitor or agonist of receptor/ligand interactions. A polynucleotide of the invention can encode a polypeptide exhibiting such characteristics. Examples of such receptors

and ligands include, without limitation, cytokine receptors and their ligands, receptor kinases and their ligands, receptor phosphatases and their ligands, receptors involved in cell-cell interactions and their ligands (including without limitation, cellular adhesion molecules (such as selectins, integrins and their ligands) and receptor/ligand pairs involved in antigen presentation, antigen recognition and development of cellular and humoral immune responses. Receptors and ligands are also useful for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction. A protein of the present invention (including, without limitation, fragments of receptors and ligands) may themselves be useful as inhibitors of receptor/ligand interactions.

The activity of a polypeptide of the invention may, among other means, be measured by the following methods:

Suitable assays for receptor-ligand activity include without limitation those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A. M. Kruisbeek, D. H. Margulies, E. M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley- Interscience (Chapter 7.28, Measurement of Cellular Adhesion under static conditions 7.28.1- 7.28.22), Takai et al., Proc. Natl. Acad. Sci. USA 84:6864-6868, 1987; Bierer et al., J. Exp. Med. 168:1145-1156, 1988; Rosenstein et al., J. Exp. Med. 169:149-160 1989; Stoltenborg et al., J. Immunol. Methods 175:59-68, 1994; Stitt et al., Cell 80:661-670, 1995.

By way of example, the polypeptides of the invention may be used as a receptor for a ligand(s) thereby transmitting the biological activity of that ligand(s). Ligands may be identified through binding assays, affinity chromatography, dihybrid screening assays, BIAcore assays, gel overlay assays, or other methods known in the art.

Studies characterizing drugs or proteins as agonist or antagonist or partial agonists or a partial antagonist require the use of other proteins as competing ligands. The polypeptides of the present invention or ligand(s) thereof may be labeled by being coupled to radioisotopes, colorimetric molecules or toxin molecules by conventional methods. ("Guide to Protein Purification" Murray P. Deutscher (ed) Methods in Enzymology Vol. 182 (1990) Academic Press, Inc. San Diego). Examples of radioisotopes include, but are not limited to, tritium and carbon-14. Examples of colorimetric molecules include, but are not limited to, fluorescent molecules such as fluorescamine, or rhodamine or other colorimetric molecules. Examples of toxins include, but are not limited, to ricin.

4.10.13 DRUG SCREENING

This invention is particularly useful for screening chemical compounds by using the novel polypeptides or binding fragments thereof in any of a variety of drug screening techniques.

The polypeptides or fragments employed in such a test may either be free in solution, affixed to a solid support, borne on a cell surface or located intracellularly. One method of drug screening utilizes eukaryotic or prokaryotic host cells which are stably transformed with recombinant nucleic acids expressing the polypeptide or a fragment thereof. Drugs are screened against such transformed cells in competitive binding assays. Such cells, either in viable or fixed form, can be used for standard binding assays. One may measure, for example, the formation of complexes between polypeptides of the invention or fragments and the agent being tested or examine the diminution in complex formation between the novel polypeptides and an appropriate cell line, which are well known in the art.

Sources for test compounds that may be screened for ability to bind to or modulate (*i.e.*, increase or decrease) the activity of polypeptides of the invention include (1) inorganic and organic chemical libraries, (2) natural product libraries, and (3) combinatorial libraries comprised of either random or mimetic peptides, oligonucleotides or organic molecules.

Chemical libraries may be readily synthesized or purchased from a number of commercial sources, and may include structural analogs of known compounds or compounds that are identified as "hits" or "leads" via natural product screening.

The sources of natural product libraries are microorganisms (including bacteria and fungi), animals, plants or other vegetation, or marine organisms, and libraries of mixtures for screening may be created by: (1) fermentation and extraction of broths from soil, plant or marine microorganisms or (2) extraction of the organisms themselves. Natural product libraries include polyketides, non-ribosomal peptides, and (non-naturally occurring) variants thereof. For a review, see *Science 282*:63-68 (1998).

Combinatorial libraries are composed of large numbers of peptides, oligonucleotides or organic compounds and can be readily prepared by traditional automated synthesis methods, PCR, cloning or proprietary synthetic methods. Of particular interest are peptide and oligonucleotide combinatorial libraries. Still other libraries of interest include peptide, protein, peptidomimetic, multiparallel synthetic collection, recombinatorial, and polypeptide libraries. For a review of combinatorial chemistry and libraries created therefrom, see Myers, *Curr. Opin. Biotechnol.* 8:701-707 (1997). For reviews and examples of peptidomimetic libraries, see Al-Obeidi et al., *Mol. Biotechnol*, 9(3):205-23 (1998); Hruby et al., *Curr Opin Chem Biol*, 1(1):114-19 (1997); Dorner et al., *Bioorg Med Chem*, 4(5):709-15 (1996) (alkylated dipeptides).

Identification of modulators through use of the various libraries described herein permits modification of the candidate "hit" (or "lead") to optimize the capacity of the "hit" to bind a polypeptide of the invention. The molecules identified in the binding assay are then tested for antagonist or agonist activity in *in vivo* tissue culture or animal models that are well known in the

art. In brief, the molecules are titrated into a plurality of cell cultures or animals and then tested for either cell/animal death or prolonged survival of the animal/cells.

The binding molecules thus identified may be complexed with toxins, *e.g.*, ricin or cholera, or with other compounds that are toxic to cells such as radioisotopes. The toxin-binding molecule complex is then targeted to a tumor or other cell by the specificity of the binding molecule for a polypeptide of the invention. Alternatively, the binding molecules may be complexed with imaging agents for targeting and imaging purposes.

4.10.14 ASSAY FOR RECEPTOR ACTIVITY

The invention also provides methods to detect specific binding of a polypeptide *e.g.* a ligand or a receptor. The art provides numerous assays particularly useful for identifying previously unknown binding partners for receptor polypeptides of the invention. For example, expression cloning using mammalian or bacterial cells, or dihybrid screening assays can be used to identify polynucleotides encoding binding partners. As another example, affinity chromatography with the appropriate immobilized polypeptide of the invention can be used to isolate polypeptides that recognize and bind polypeptides of the invention. There are a number of different libraries used for the identification of compounds, and in particular small molecules, that modulate (*i.e.*, increase or decrease) biological activity of a polypeptide of the invention. Ligands for receptor polypeptides of the invention can also be identified by adding exogenous ligands, or cocktails of ligands to two cells populations that are genetically identical except for the expression of the receptor of the invention: one cell population expresses the receptor of the invention whereas the other does not. The responses of the two cell populations to the addition of ligands(s) are then compared. Alternatively, an expression library can be co-expressed with the polypeptide of the invention in cells and assayed for an autocrine response to identify potential ligand(s). As still another example, BIAcore assays, gel overlay assays, or other methods known in the art can be used to identify binding partner polypeptides, including, (1) organic and inorganic chemical libraries, (2) natural product libraries, and (3) combinatorial libraries comprised of random peptides, oligonucleotides or organic molecules.

The role of downstream intracellular signaling molecules in the signaling cascade of the polypeptide of the invention can be determined. For example, a chimeric protein in which the cytoplasmic domain of the polypeptide of the invention is fused to the extracellular portion of a protein, whose ligand has been identified, is produced in a host cell. The cell is then incubated with the ligand specific for the extracellular portion of the chimeric protein, thereby activating the chimeric receptor. Known downstream proteins involved in intracellular signaling can then

be assayed for expected modifications *i.e.* phosphorylation. Other methods known to those in the art can also be used to identify signaling molecules involved in receptor activity.

4.10.15 ANTI-INFLAMMATORY ACTIVITY

Compositions of the present invention may also exhibit anti-inflammatory activity. The anti-inflammatory activity may be achieved by providing a stimulus to cells involved in the inflammatory response, by inhibiting or promoting cell-cell interactions (such as, for example, cell adhesion), by inhibiting or promoting chemotaxis of cells involved in the inflammatory process, inhibiting or promoting cell extravasation, or by stimulating or suppressing production of other factors which more directly inhibit or promote an inflammatory response. Compositions with such activities can be used to treat inflammatory conditions including chronic or acute conditions), including without limitation intimation associated with infection (such as septic shock, sepsis or systemic inflammatory response syndrome (SIRS)), ischemia-reperfusion injury, endotoxin lethality, arthritis, complement-mediated hyperacute rejection, nephritis, cytokine or chemokine-induced lung injury, inflammatory bowel disease, Crohn's disease or resulting from over production of cytokines such as TNF or IL-1. Compositions of the invention may also be useful to treat anaphylaxis and hypersensitivity to an antigenic substance or material. Compositions of this invention may be utilized to prevent or treat conditions such as, but not limited to, sepsis, acute pancreatitis, endotoxin shock, cytokine induced shock, rheumatoid arthritis, chronic inflammatory arthritis, pancreatic cell damage from diabetes mellitus type 1, graft versus host disease, inflammatory bowel disease, inflamation associated with pulmonary disease, other autoimmune disease or inflammatory disease, an antiproliferative agent such as for acute or chronic mylegenous leukemia or in the prevention of premature labor secondary to intrauterine infections.

4.10.16 LEUKEMIAS

Leukemias and related disorders may be treated or prevented by administration of a therapeutic that promotes or inhibits function of the polynucleotides and/or polypeptides of the invention. Such leukemias and related disorders include but are not limited to acute leukemia, acute lymphocytic leukemia, acute myelocytic leukemia, myeloblastic, promyelocytic, myelomonocytic, monocytic, erythroleukemia, chronic leukemia, chronic myelocytic (granulocytic) leukemia and chronic lymphocytic leukemia (for a review of such disorders, see Fishman et al., 1985, Medicine, 2d Ed., J.B. Lippincott Co., Philadelphia).

4.10.17 NERVOUS SYSTEM DISORDERS

Nervous system disorders, involving cell types which can be tested for efficacy of intervention with compounds that modulate the activity of the polynucleotides and/or polypeptides of the invention, and which can be treated upon thus observing an indication of therapeutic utility, include but are not limited to nervous system injuries, and diseases or disorders which result in either a disconnection of axons, a diminution or degeneration of neurons, or demyelination. Nervous system lesions which may be treated in a patient (including human and non-human mammalian patients) according to the invention include but are not limited to the following lesions of either the central (including spinal cord, brain) or peripheral nervous systems:

(i) traumatic lesions, including lesions caused by physical injury or associated with surgery, for example, lesions which sever a portion of the nervous system, or compression injuries;

(ii) ischemic lesions, in which a lack of oxygen in a portion of the nervous system results in neuronal injury or death, including cerebral infarction or ischemia, or spinal cord infarction or ischemia;

(iii) infectious lesions, in which a portion of the nervous system is destroyed or injured as a result of infection, for example, by an abscess or associated with infection by human immunodeficiency virus, herpes zoster, or herpes simplex virus or with Lyme disease, tuberculosis, syphilis;

(iv) degenerative lesions, in which a portion of the nervous system is destroyed or injured as a result of a degenerative process including but not limited to degeneration associated with Parkinson's disease, Alzheimer's disease, Huntington's chorea, or amyotrophic lateral sclerosis;

(v) lesions associated with nutritional diseases or disorders, in which a portion of the nervous system is destroyed or injured by a nutritional disorder or disorder of metabolism including but not limited to, vitamin B12 deficiency, folic acid deficiency, Wernicke disease, tobacco-alcohol amblyopia, Marchiafava-Bignami disease (primary degeneration of the corpus callosum), and alcoholic cerebellar degeneration;

(vi) neurological lesions associated with systemic diseases including but not limited to diabetes (diabetic neuropathy, Bell's palsy), systemic lupus erythematosus, carcinoma, or sarcoidosis;

(vii) lesions caused by toxic substances including alcohol, lead, or particular neurotoxins; and

(viii) demyelinated lesions in which a portion of the nervous system is destroyed or injured by a demyelinating disease including but not limited to multiple sclerosis, human

immunodeficiency virus-associated myelopathy, transverse myelopathy or various etiologies, progressive multifocal leukoencephalopathy, and central pontine myelinolysis.

Therapeutics which are useful according to the invention for treatment of a nervous system disorder may be selected by testing for biological activity in promoting the survival or differentiation of neurons. For example, and not by way of limitation, therapeutics which elicit any of the following effects may be useful according to the invention:

(i) increased survival time of neurons in culture;

(ii) increased sprouting of neurons in culture or in vivo;

(iii) increased production of a neuron-associated molecule in culture or *in vivo, e.g.*, choline acetyltransferase or acetylcholinesterase with respect to motor neurons; or

(iv) decreased symptoms of neuron dysfunction in vivo.

Such effects may be measured by any method known in the art. In preferred, non-limiting embodiments, increased survival of neurons may be measured by the method set forth in Arakawa et al. (1990, J. Neurosci. 10:3507-3515); increased sprouting of neurons may be detected by methods set forth in Pestronk et al. (1980, Exp. Neurol. 70:65-82) or Brown et al. (1981, Ann. Rev. Neurosci. 4:17-42); increased production of neuron-associated molecules may be measured by bioassay, enzymatic assay, antibody binding, Northern blot assay, *etc.*, depending on the molecule to be measured; and motor neuron dysfunction may be measured by assessing the physical manifestation of motor neuron disorder, *e.g.*, weakness, motor neuron conduction velocity, or functional disability.

In specific embodiments, motor neuron disorders that may be treated according to the invention include but are not limited to disorders such as infarction, infection, exposure to toxin, trauma, surgical damage, degenerative disease or malignancy that may affect motor neurons as well as other components of the nervous system, as well as disorders that selectively affect neurons such as amyotrophic lateral sclerosis, and including but not limited to progressive spinal muscular atrophy, progressive bulbar palsy, primary lateral sclerosis, infantile and juvenile muscular atrophy, progressive bulbar paralysis of childhood (Fazio-Londe syndrome), poliomyelitis and the post polio syndrome, and Hereditary Motorsensory Neuropathy (Charcot-Marie-Tooth Disease).

4.10.18 OTHER ACTIVITIES

A polypeptide of the invention may also exhibit one or more of the following additional activities or effects: inhibiting the growth, infection or function of, or killing, infectious agents, including, without limitation, bacteria, viruses, fungi and other parasites; effecting (suppressing or enhancing) bodily characteristics, including, without limitation, height, weight, hair color, eye

color, skin, fat to lean ratio or other tissue pigmentation, or organ or body part size or shape (such as, for example, breast augmentation or diminution, change in bone form or shape); effecting biorhythms or circadian cycles or rhythms; effecting the fertility of male or female subjects; effecting the metabolism, catabolism, anabolism, processing, utilization, storage or elimination of dietary fat, lipid, protein, carbohydrate, vitamins, minerals, co-factors or other nutritional factors or component(s); effecting behavioral characteristics, including, without limitation, appetite, libido, stress, cognition (including cognitive disorders), depression (including depressive disorders) and violent behaviors; providing analgesic effects or other pain reducing effects; promoting differentiation and growth of embryonic stem cells in lineages other than hematopoietic lineages; hormonal or endocrine activity; in the case of enzymes, correcting deficiencies of the enzyme and treating deficiency-related diseases; treatment of hyperproliferative disorders (such as, for example, psoriasis); immunoglobulin-like activity (such as, for example, the ability to bind antigens or complement); and the ability to act as an antigen in a vaccine composition to raise an immune response against such protein or another material or entity which is cross-reactive with such protein.

4.10.19 IDENTIFICATION OF POLYMORPHISMS

The demonstration of polymorphisms makes possible the identification of such polymorphisms in human subjects and the pharmacogenetic use of this information for diagnosis and treatment. Such polymorphisms may be associated with, *e.g.*, differential predisposition or susceptibility to various disease states (such as disorders involving inflammation or immune response) or a differential response to drug administration, and this genetic information can be used to tailor preventive or therapeutic treatment appropriately. For example, the existence of a polymorphism associated with a predisposition to inflammation or autoimmune disease makes possible the diagnosis of this condition in humans by identifying the presence of the polymorphism.

Polymorphisms can be identified in a variety of ways known in the art which all generally involve obtaining a sample from a patient, analyzing DNA from the sample, optionally involving isolation or amplification of the DNA, and identifying the presence of the polymorphism in the DNA. For example, PCR may be used to amplify an appropriate fragment of genomic DNA which may then be sequenced. Alternatively, the DNA may be subjected to allele-specific oligonucleotide hybridization (in which appropriate oligonucleotides are hybridized to the DNA under conditions permitting detection of a single base mismatch) or to a single nucleotide extension assay (in which an oligonucleotide that hybridizes immediately adjacent to the position of the polymorphism is extended with one or more labeled nucleotides).

In addition, traditional restriction fragment length polymorphism analysis (using restriction enzymes that provide differential digestion of the genomic DNA depending on the presence or absence of the polymorphism) may be performed. Arrays with nucleotide sequences of the present invention can be used to detect polymorphisms. The array can comprise modified nucleotide sequences of the present invention in order to detect the nucleotide sequences of the present invention. In the alternative, any one of the nucleotide sequences of the present invention can be placed on the array to detect changes from those sequences.

Alternatively a polymorphism resulting in a change in the amino acid sequence could also be detected by detecting a corresponding change in amino acid sequence of the protein, *e.g.*, by an antibody specific to the variant sequence.

4.10.20 ARTHRITIS AND INFLAMMATION

The immunosuppressive effects of the compositions of the invention against rheumatoid arthritis are determined in an experimental animal model system. The experimental model system is adjuvant induced arthritis in rats, and the protocol is described by J. Holoshitz, et at., 1983, Science, 219:56, or by B. Waksman et al., 1963, Int. Arch. Allergy Appl. Immunol., 23:129. Induction of the disease can be caused by a single injection, generally intradermally, of a suspension of killed Mycobacterium tuberculosis in complete Freund's adjuvant (CFA). The route of injection can vary, but rats may be injected at the base of the tail with an adjuvant mixture. The polypeptide is administered in phosphate buffered solution (PBS) at a dose of about 1-5 mg/kg. The control consists of administering PBS only.

The procedure for testing the effects of the test compound would consist of intradermally injecting killed Mycobacterium tuberculosis in CFA followed by immediately administering the test compound and subsequent treatment every other day until day 24. At 14, 15, 18, 20, 22, and 24 days after injection of Mycobacterium CFA, an overall arthritis score may be obtained as described by J. Holoskitz above. An analysis of the data would reveal that the test compound would have a dramatic affect on the swelling of the joints as measured by a decrease of the arthritis score.

4.11 THERAPEUTIC METHODS

The compositions (including polypeptide fragments, analogs, variants and antibodies or other binding partners or modulators including antisense polynucleotides) of the invention have numerous applications in a variety of therapeutic methods. Examples of therapeutic applications include, but are not limited to, those exemplified herein.

4.11.1 EXAMPLE

One embodiment of the invention is the administration of an effective amount of the polypeptides or other composition of the invention to individuals affected by a disease or disorder that can be modulated by regulating the peptides of the invention. While the mode of administration is not particularly important, parenteral administration is preferred. An exemplary mode of administration is to deliver an intravenous bolus. The dosage of the polypeptides or other composition of the invention will normally be determined by the prescribing physician. It is to be expected that the dosage will vary according to the age, weight, condition and response of the individual patient. Typically, the amount of polypeptide administered per dose will be in the range of about 0.01μg/kg to 100 mg/kg of body weight, with the preferred dose being about 0.1μg/kg to 10 mg/kg of patient body weight. For parenteral administration, polypeptides of the invention will be formulated in an injectable form combined with a pharmaceutically acceptable parenteral vehicle. Such vehicles are well known in the art and examples include water, saline, Ringer's solution, dextrose solution, and solutions consisting of small amounts of the human serum albumin. The vehicle may contain minor amounts of additives that maintain the isotonicity and stability of the polypeptide or other active ingredient. The preparation of such solutions is within the skill of the art.

4.12 PHARMACEUTICAL FORMULATIONS AND ROUTES OF ADMINISTRATION

A protein or other composition of the present invention (from whatever source derived, including without limitation from recombinant and non-recombinant sources and including antibodies and other binding partners of the polypeptides of the invention) may be administered to a patient in need, by itself, or in pharmaceutical compositions where it is mixed with suitable carriers or excipient(s) at doses to treat or ameliorate a variety of disorders. Such a composition may optionally contain (in addition to protein or other active ingredient and a carrier) diluents, fillers, salts, buffers, stabilizers, solubilizers, and other materials well known in the art. The term "pharmaceutically acceptable" means a non-toxic material that does not interfere with the effectiveness of the biological activity of the active ingredient(s). The characteristics of the carrier will depend on the route of administration. The pharmaceutical composition of the invention may also contain cytokines, lymphokines, or other hematopoietic factors such as M-CSF, GM-CSF, TNF, IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, IL-14, IL-15, IFN, TNF0, TNF1, TNF2, G-CSF, Meg-CSF, thrombopoietin, stem cell factor, and erythropoietin. In further compositions, proteins of the invention may be combined with other agents beneficial to the treatment of the disease or disorder in question. These agents

include various growth factors such as epidermal growth factor (EGF), platelet-derived growth factor (PDGF), transforming growth factors (TGF-α and TGF-β), insulin-like growth factor (IGF), as well as cytokines described herein.

The pharmaceutical composition may further contain other agents which either enhance the activity of the protein or other active ingredient or complement its activity or use in treatment. Such additional factors and/or agents may be included in the pharmaceutical composition to produce a synergistic effect with protein or other active ingredient of the invention, or to minimize side effects. Conversely, protein or other active ingredient of the present invention may be included in formulations of the particular clotting factor, cytokine, lymphokine, other hematopoietic factor, thrombolytic or anti-thrombotic factor, or anti-inflammatory agent to minimize side effects of the clotting factor, cytokine, lymphokine, other hematopoietic factor, thrombolytic or anti-thrombotic factor, or anti-inflammatory agent (such as IL-1Ra, IL-1 Hy1, IL-1 Hy2, anti-TNF, corticosteroids, immunosuppressive agents). A protein of the present invention may be active in multimers (*e.g.*, heterodimers or homodimers) or complexes with itself or other proteins. As a result, pharmaceutical compositions of the invention may comprise a protein of the invention in such multimeric or complexed form.

As an alternative to being included in a pharmaceutical composition of the invention including a first protein, a second protein or a therapeutic agent may be concurrently administered with the first protein (*e.g.*, at the same time, or at differing times provided that therapeutic concentrations of the combination of agents is achieved at the treatment site). Techniques for formulation and administration of the compounds of the instant application may be found in "Remington's Pharmaceutical Sciences," Mack Publishing Co., Easton, PA, latest edition. A therapeutically effective dose further refers to that amount of the compound sufficient to result in amelioration of symptoms, *e.g.*, treatment, healing, prevention or amelioration of the relevant medical condition, or an increase in rate of treatment, healing, prevention or amelioration of such conditions. When applied to an individual active ingredient, administered alone, a therapeutically effective dose refers to that ingredient alone. When applied to a combination, a therapeutically effective dose refers to combined amounts of the active ingredients that result in the therapeutic effect, whether administered in combination, serially or simultaneously.

In practicing the method of treatment or use of the present invention, a therapeutically effective amount of protein or other active ingredient of the present invention is administered to a mammal having a condition to be treated. Protein or other active ingredient of the present invention may be administered in accordance with the method of the invention either alone or in combination with other therapies such as treatments employing cytokines, lymphokines or other

hematopoietic factors. When co- administered with one or more cytokines, lymphokines or other hematopoietic factors, protein or other active ingredient of the present invention may be administered either simultaneously with the cytokine(s), lymphokine(s), other hematopoietic factor(s), thrombolytic or anti-thrombotic factors, or sequentially. If administered sequentially, the attending physician will decide on the appropriate sequence of administering protein or other active ingredient of the present invention in combination with cytokine(s), lymphokine(s), other hematopoietic factor(s), thrombolytic or anti-thrombotic factors.

4.12.1 ROUTES OF ADMINISTRATION

Suitable routes of administration may, for example, include oral, rectal, transmucosal, or intestinal administration; parenteral delivery, including intramuscular, subcutaneous, intramedullary injections, as well as intrathecal, direct intraventricular, intravenous, intraperitoneal, intranasal, or intraocular injections. Administration of protein or other active ingredient of the present invention used in the pharmaceutical composition or to practice the method of the present invention can be carried out in a variety of conventional ways, such as oral ingestion, inhalation, topical application or cutaneous, subcutaneous, intraperitoneal, parenteral or intravenous injection. Intravenous administration to the patient is preferred.

Alternately, one may administer the compound in a local rather than systemic manner, for example, via injection of the compound directly into a arthritic joints or in fibrotic tissue, often in a depot or sustained release formulation. In order to prevent the scarring process frequently occurring as complication of glaucoma surgery, the compounds may be administered topically, for example, as eye drops. Furthermore, one may administer the drug in a targeted drug delivery system, for example, in a liposome coated with a specific antibody, targeting, for example, arthritic or fibrotic tissue. The liposomes will be targeted to and taken up selectively by the afflicted tissue.

The polypeptides of the invention are administered by any route that delivers an effective dosage to the desired site of action. The determination of a suitable route of administration and an effective dosage for a particular indication is within the level of skill in the art. Preferably for wound treatment, one administers the therapeutic compound directly to the site. Suitable dosage ranges for the polypeptides of the invention can be extrapolated from these dosages or from similar studies in appropriate animal models. Dosages can then be adjusted as necessary by the clinician to provide maximal therapeutic benefit.

4.12.2 COMPOSITIONS/FORMULATIONS

Pharmaceutical compositions for use in accordance with the present invention thus may be formulated in a conventional manner using one or more physiologically acceptable carriers comprising excipients and auxiliaries which facilitate processing of the active compounds into preparations which can be used pharmaceutically. These pharmaceutical compositions may be manufactured in a manner that is itself known, *e.g.*, by means of conventional mixing, dissolving, granulating, dragee-making, levigating, emulsifying, encapsulating, entrapping or lyophilizing processes. Proper formulation is dependent upon the route of administration chosen. When a therapeutically effective amount of protein or other active ingredient of the present invention is administered orally, protein or other active ingredient of the present invention will be in the form of a tablet, capsule, powder, solution or elixir. When administered in tablet form, the pharmaceutical composition of the invention may additionally contain a solid carrier such as a gelatin or an adjuvant. The tablet, capsule, and powder contain from about 5 to 95% protein or other active ingredient of the present invention, and preferably from about 25 to 90% protein or other active ingredient of the present invention. When administered in liquid form, a liquid carrier such as water, petroleum, oils of animal or plant origin such as peanut oil, mineral oil, soybean oil, or sesame oil, or synthetic oils may be added. The liquid form of the pharmaceutical composition may further contain physiological saline solution, dextrose or other saccharide solution, or glycols such as ethylene glycol, propylene glycol or polyethylene glycol. When administered in liquid form, the pharmaceutical composition contains from about 0.5 to 90% by weight of protein or other active ingredient of the present invention, and preferably from about 1 to 50% protein or other active ingredient of the present invention.

When a therapeutically effective amount of protein or other active ingredient of the present invention is administered by intravenous, cutaneous or subcutaneous injection, protein or other active ingredient of the present invention will be in the form of a pyrogen-free, parenterally acceptable aqueous solution. The preparation of such parenterally acceptable protein or other active ingredient solutions, having due regard to pH, isotonicity, stability, and the like, is within the skill in the art. A preferred pharmaceutical composition for intravenous, cutaneous, or subcutaneous injection should contain, in addition to protein or other active ingredient of the present invention, an isotonic vehicle such as Sodium Chloride Injection, Ringer's Injection, Dextrose Injection, Dextrose and Sodium Chloride Injection, Lactated Ringer's Injection, or other vehicle as known in the art. The pharmaceutical composition of the present invention may also contain stabilizers, preservatives, buffers, antioxidants, or other additives known to those of skill in the art. For injection, the agents of the invention may be formulated in aqueous solutions, preferably in physiologically compatible buffers such as Hanks's solution, Ringer's solution, or physiological saline buffer. For transmucosal administration, penetrants appropriate

to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art.

For oral administration, the compounds can be formulated readily by combining the active compounds with pharmaceutically acceptable carriers well known in the art. Such carriers enable the compounds of the invention to be formulated as tablets, pills, dragees, capsules, liquids, gels, syrups, slurries, suspensions and the like, for oral ingestion by a patient to be treated. Pharmaceutical preparations for oral use can be obtained from a solid excipient, optionally grinding a resulting mixture, and processing the mixture of granules, after adding suitable auxiliaries, if desired, to obtain tablets or dragee cores. Suitable excipients are, in particular, fillers such as sugars, including lactose, sucrose, mannitol, or sorbitol; cellulose preparations such as, for example, maize starch, wheat starch, rice starch, potato starch, gelatin, gum tragacanth, methyl cellulose, hydroxypropylmethyl-cellulose, sodium carboxymethylcellulose, and/or polyvinylpyrrolidone (PVP). If desired, disintegrating agents may be added, such as the cross-linked polyvinyl pyrrolidone, agar, or alginic acid or a salt thereof such as sodium alginate. Dragee cores are provided with suitable coatings. For this purpose, concentrated sugar solutions may be used, which may optionally contain gum arabic, talc, polyvinyl pyrrolidone, carbopol gel, polyethylene glycol, and/or titanium dioxide, lacquer solutions, and suitable organic solvents or solvent mixtures. Dyestuffs or pigments may be added to the tablets or dragee coatings for identification or to characterize different combinations of active compound doses.

Pharmaceutical preparations which can be used orally include push-fit capsules made of gelatin, as well as soft, sealed capsules made of gelatin and a plasticizer, such as glycerol or sorbitol. The push-fit capsules can contain the active ingredients in admixture with filler such as lactose, binders such as starches, and/or lubricants such as talc or magnesium stearate and, optionally, stabilizers. In soft capsules, the active compounds may be dissolved or suspended in suitable liquids, such as fatty oils, liquid paraffin, or liquid polyethylene glycols. In addition, stabilizers may be added. All formulations for oral administration should be in dosages suitable for such administration. For buccal administration, the compositions may take the form of tablets or lozenges formulated in conventional manner.

For administration by inhalation, the compounds for use according to the present invention are conveniently delivered in the form of an aerosol spray presentation from pressurized packs or a nebuliser, with the use of a suitable propellant, *e.g.*, dichlorodifluoromethane, trichlorofluoromethane, dichlorotetrafluoroethane, carbon dioxide or other suitable gas. In the case of a pressurized aerosol the dosage unit may be determined by providing a valve to deliver a metered amount. Capsules and cartridges of, *e.g.*, gelatin for use

in an inhaler or insufflator may be formulated containing a powder mix of the compound and a suitable powder base such as lactose or starch. The compounds may be formulated for parenteral administration by injection, *e.g.*, by bolus injection or continuous infusion. Formulations for injection may be presented in unit dosage form, *e.g.*, in ampules or in multi-dose containers, with an added preservative. The compositions may take such forms as suspensions, solutions or emulsions in oily or aqueous vehicles, and may contain formulatory agents such as suspending, stabilizing and/or dispersing agents.

Pharmaceutical formulations for parenteral administration include aqueous solutions of the active compounds in water-soluble form. Additionally, suspensions of the active compounds may be prepared as appropriate oily injection suspensions. Suitable lipophilic solvents or vehicles include fatty oils such as sesame oil, or synthetic fatty acid esters, such as ethyl oleate or triglycerides, or liposomes. Aqueous injection suspensions may contain substances which increase the viscosity of the suspension, such as sodium carboxymethyl cellulose, sorbitol, or dextran. Optionally, the suspension may also contain suitable stabilizers or agents which increase the solubility of the compounds to allow for the preparation of highly concentrated solutions. Alternatively, the active ingredient may be in powder form for constitution with a suitable vehicle, *e.g.*, sterile pyrogen-free water, before use.

The compounds may also be formulated in rectal compositions such as suppositories or retention enemas, *e.g.*, containing conventional suppository bases such as cocoa butter or other glycerides. In addition to the formulations described previously, the compounds may also be formulated as a depot preparation. Such long acting formulations may be administered by implantation (for example subcutaneously or intramuscularly) or by intramuscular injection. Thus, for example, the compounds may be formulated with suitable polymeric or hydrophobic materials (for example as an emulsion in an acceptable oil) or ion exchange resins, or as sparingly soluble derivatives, for example, as a sparingly soluble salt.

A pharmaceutical carrier for the hydrophobic compounds of the invention is a co-solvent system comprising benzyl alcohol, a nonpolar surfactant, a water-miscible organic polymer, and an aqueous phase. The co-solvent system may be the VPD co-solvent system. VPD is a solution of 3% w/v benzyl alcohol, 8% w/v of the nonpolar surfactant polysorbate 80, and 65% w/v polyethylene glycol 300, made up to volume in absolute ethanol. The VPD co-solvent system (VPD:5W) consists of VPD diluted 1:1 with a 5% dextrose in water solution. This co-solvent system dissolves hydrophobic compounds well, and itself produces low toxicity upon systemic administration. Naturally, the proportions of a co-solvent system may be varied considerably without destroying its solubility and toxicity characteristics. Furthermore, the identity of the co-solvent components may be varied: for example, other low-toxicity nonpolar surfactants may

be used instead of polysorbate 80; the fraction size of polyethylene glycol may be varied; other biocompatible polymers may replace polyethylene glycol, *e.g.* polyvinyl pyrrolidone; and other sugars or polysaccharides may substitute for dextrose. Alternatively, other delivery systems for hydrophobic pharmaceutical compounds may be employed. Liposomes and emulsions are well known examples of delivery vehicles or carriers for hydrophobic drugs. Certain organic solvents such as dimethylsulfoxide also may be employed, although usually at the cost of greater toxicity. Additionally, the compounds may be delivered using a sustained-release system, such as semipermeable matrices of solid hydrophobic polymers containing the therapeutic agent. Various types of sustained-release materials have been established and are well known by those skilled in the art. Sustained-release capsules may, depending on their chemical nature, release the compounds for a few weeks up to over 100 days. Depending on the chemical nature and the biological stability of the therapeutic reagent, additional strategies for protein or other active ingredient stabilization may be employed.

The pharmaceutical compositions also may comprise suitable solid or gel phase carriers or excipients. Examples of such carriers or excipients include but are not limited to calcium carbonate, calcium phosphate, various sugars, starches, cellulose derivatives, gelatin, and polymers such as polyethylene glycols. Many of the active ingredients of the invention may be provided as salts with pharmaceutically compatible counter ions. Such pharmaceutically acceptable base addition salts are those salts which retain the biological effectiveness and properties of the free acids and which are obtained by reaction with inorganic or organic bases such as sodium hydroxide, magnesium hydroxide, ammonia, trialkylamine, dialkylamine, monoalkylamine, dibasic amino acids, sodium acetate, potassium benzoate, triethanol amine and the like.

The pharmaceutical composition of the invention may be in the form of a complex of the protein(s) or other active ingredient(s) of present invention along with protein or peptide antigens. The protein and/or peptide antigen will deliver a stimulatory signal to both B and T lymphocytes. B-lymphocytes will respond to antigen through their surface immunoglobulin receptor. T lymphocytes will respond to antigen through the T cell receptor (TCR) following presentation of the antigen by MHC proteins. MHC and structurally related proteins including those encoded by class I and class II MHC genes on host cells will serve to present the peptide antigen(s) to T lymphocytes. The antigen components could also be supplied as purified MHC-peptide complexes alone or with co-stimulatory molecules that can directly signal T cells. Alternatively antibodies able to bind surface immunoglobulin and other molecules on B cells as well as antibodies able to bind the TCR and other molecules on T cells can be combined with the pharmaceutical composition of the invention.

The pharmaceutical composition of the invention may be in the form of a liposome in which protein of the present invention is combined, in addition to other pharmaceutically acceptable carriers, with amphipathic agents such as lipids which exist in aggregated form as micelles, insoluble monolayers, liquid crystals, or lamellar layers in aqueous solution. Suitable lipids for liposomal formulation include, without limitation, monoglycerides, diglycerides, sulfatides, lysolecithins, phospholipids, saponin, bile acids, and the like. Preparation of such liposomal formulations is within the level of skill in the art, as disclosed, for example, in U.S. Patent Nos. 4,235,871; 4,501,728; 4,837,028; and 4,737,323, all of which are incorporated herein by reference.

The amount of protein or other active ingredient of the present invention in the pharmaceutical composition of the present invention will depend upon the nature and severity of the condition being treated, and on the nature of prior treatments which the patient has undergone. Ultimately, the attending physician will decide the amount of protein or other active ingredient of the present invention with which to treat each individual patient. Initially, the attending physician will administer low doses of protein or other active ingredient of the present invention and observe the patient's response. Larger doses of protein or other active ingredient of the present invention may be administered until the optimal therapeutic effect is obtained for the patient, and at that point the dosage is not increased further. It is contemplated that the various pharmaceutical compositions used to practice the method of the present invention should contain about 0.01 μg to about 100 mg (preferably about 0.1 μg to about 10 mg, more preferably about 0.1 μg to about 1 mg) of protein or other active ingredient of the present invention per kg body weight. For compositions of the present invention which are useful for bone, cartilage, tendon or ligament regeneration, the therapeutic method includes administering the composition topically, systematically, or locally as an implant or device. When administered, the therapeutic composition for use in this invention is, of course, in a pyrogen-free, physiologically acceptable form. Further, the composition may desirably be encapsulated or injected in a viscous form for delivery to the site of bone, cartilage or tissue damage. Topical administration may be suitable for wound healing and tissue repair. Therapeutically useful agents other than a protein or other active ingredient of the invention which may also optionally be included in the composition as described above, may alternatively or additionally, be administered simultaneously or sequentially with the composition in the methods of the invention. Preferably for bone and/or cartilage formation, the composition would include a matrix capable of delivering the protein-containing or other active ingredient-containing composition to the site of bone and/or cartilage damage, providing a structure for the developing bone and cartilage and optimally

capable of being resorbed into the body. Such matrices may be formed of materials presently in use for other implanted medical applications.

The choice of matrix material is based on biocompatibility, biodegradability, mechanical properties, cosmetic appearance and interface properties. The particular application of the compositions will define the appropriate formulation. Potential matrices for the compositions may be biodegradable and chemically defined calcium sulfate, tricalcium phosphate, hydroxyapatite, polylactic acid, polyglycolic acid and polyanhydrides. Other potential materials are biodegradable and biologically well-defined, such as bone or dermal collagen. Further matrices are comprised of pure proteins or extracellular matrix components. Other potential matrices are nonbiodegradable and chemically defined, such as sintered hydroxyapatite, bioglass, aluminates, or other ceramics. Matrices may be comprised of combinations of any of the above-mentioned types of material, such as polylactic acid and hydroxyapatite or collagen and tricalcium phosphate. The bioceramics may be altered in composition, such as in calcium-aluminate-phosphate and processing to alter pore size, particle size, particle shape, and biodegradability. Presently preferred is a 50:50 (mole weight) copolymer of lactic acid and glycolic acid in the form of porous particles having diameters ranging from 150 to 800 microns. In some applications, it will be useful to utilize a sequestering agent, such as carboxymethyl cellulose or autologous blood clot, to prevent the protein compositions from disassociating from the matrix.

A preferred family of sequestering agents is cellulosic materials such as alkylcelluloses (including hydroxyalkylcelluloses), including methylcellulose, ethylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxypropyl-methylcellulose, and carboxymethylcellulose, the most preferred being cationic salts of carboxymethylcellulose (CMC). Other preferred sequestering agents include hyaluronic acid, sodium alginate, poly(ethylene glycol), polyoxyethylene oxide, carboxyvinyl polymer and poly(vinyl alcohol). The amount of sequestering agent useful herein is 0.5-20 wt %, preferably 1-10 wt % based on total formulation weight, which represents the amount necessary to prevent desorption of the protein from the polymer matrix and to provide appropriate handling of the composition, yet not so much that the progenitor cells are prevented from infiltrating the matrix, thereby providing the protein the opportunity to assist the osteogenic activity of the progenitor cells. In further compositions, proteins or other active ingredients of the invention may be combined with other agents beneficial to the treatment of the bone and/or cartilage defect, wound, or tissue in question. These agents include various growth factors such as epidermal growth factor (EGF), platelet derived growth factor (PDGF), transforming growth factors (TGF-α and TGF-β), and insulin-like growth factor (IGF).

The therapeutic compositions are also presently valuable for veterinary applications. Particularly domestic animals and thoroughbred horses, in addition to humans, are desired patients for such treatment with proteins or other active ingredients of the present invention. The dosage regimen of a protein-containing pharmaceutical composition to be used in tissue regeneration will be determined by the attending physician considering various factors which modify the action of the proteins, *e.g.*, amount of tissue weight desired to be formed, the site of damage, the condition of the damaged tissue, the size of a wound, type of damaged tissue (*e.g.*, bone), the patient's age, sex, and diet, the severity of any infection, time of administration and other clinical factors. The dosage may vary with the type of matrix used in the reconstitution and with inclusion of other proteins in the pharmaceutical composition. For example, the addition of other known growth factors, such as IGF I (insulin like growth factor I), to the final composition, may also effect the dosage. Progress can be monitored by periodic assessment of tissue/bone growth and/or repair, for example, X-rays, histomorphometric determinations and tetracycline labeling.

Polynucleotides of the present invention can also be used for gene therapy. Such polynucleotides can be introduced either in vivo or ex vivo into cells for expression in a mammalian subject. Polynucleotides of the invention may also be administered by other known methods for introduction of nucleic acid into a cell or organism (including, without limitation, in the form of viral vectors or naked DNA). Cells may also be cultured ex vivo in the presence of proteins of the present invention in order to proliferate or to produce a desired effect on or activity in such cells. Treated cells can then be introduced in vivo for therapeutic purposes.

4.12.3 EFFECTIVE DOSAGE

Pharmaceutical compositions suitable for use in the present invention include compositions wherein the active ingredients are contained in an effective amount to achieve its intended purpose. More specifically, a therapeutically effective amount means an amount effective to prevent development of or to alleviate the existing symptoms of the subject being treated. Determination of the effective amount is well within the capability of those skilled in the art, especially in light of the detailed disclosure provided herein. For any compound used in the method of the invention, the therapeutically effective dose can be estimated initially from appropriate in vitro assays. For example, a dose can be formulated in animal models to achieve a circulating concentration range that can be used to more accurately determine useful doses in humans. For example, a dose can be formulated in animal models to achieve a circulating concentration range that includes the IC_{50} as determined in cell culture (*i.e.*, the concentration of

the test compound which achieves a half-maximal inhibition of the protein's biological activity). Such information can be used to more accurately determine useful doses in humans.

A therapeutically effective dose refers to that amount of the compound that results in amelioration of symptoms or a prolongation of survival in a patient. Toxicity and therapeutic efficacy of such compounds can be determined by standard pharmaceutical procedures in cell cultures or experimental animals, *e.g.*, for determining the LD_{50} (the dose lethal to 50% of the population) and the ED_{50} (the dose therapeutically effective in 50% of the population). The dose ratio between toxic and therapeutic effects is the therapeutic index and it can be expressed as the ratio between LD_{50} and ED_{50}. Compounds which exhibit high therapeutic indices are preferred. The data obtained from these cell culture assays and animal studies can be used in formulating a range of dosage for use in human. The dosage of such compounds lies preferably within a range of circulating concentrations that include the ED_{50} with little or no toxicity. The dosage may vary within this range depending upon the dosage form employed and the route of administration utilized. The exact formulation, route of administration and dosage can be chosen by the individual physician in view of the patient's condition. See, *e.g.*, Fingl et al., 1975, in "The Pharmacological Basis of Therapeutics", Ch. 1 p.1. Dosage amount and interval may be adjusted individually to provide plasma levels of the active moiety which are sufficient to maintain the desired effects, or minimal effective concentration (MEC). The MEC will vary for each compound but can be estimated from *in vitro* data. Dosages necessary to achieve the MEC will depend on individual characteristics and route of administration. However, HPLC assays or bioassays can be used to determine plasma concentrations.

Dosage intervals can also be determined using MEC value. Compounds should be administered using a regimen that maintains plasma levels above the MEC for 10-90% of the time, preferably between 30-90% and most preferably between 50-90%. In cases of local administration or selective uptake, the effective local concentration of the drug may not be related to plasma concentration.

An exemplary dosage regimen for polypeptides or other compositions of the invention will be in the range of about 0.01 μg/kg to 100 mg/kg of body weight daily, with the preferred dose being about 0.1 μg/kg to 25 mg/kg of patient body weight daily, varying in adults and children. Dosing may be once daily, or equivalent doses may be delivered at longer or shorter intervals.

The amount of composition administered will, of course, be dependent on the subject being treated, on the subject's age and weight, the severity of the affliction, the manner of administration and the judgment of the prescribing physician.

4.12.4 PACKAGING

The compositions may, if desired, be presented in a pack or dispenser device which may contain one or more unit dosage forms containing the active ingredient. The pack may, for example, comprise metal or plastic foil, such as a blister pack. The pack or dispenser device may be accompanied by instructions for administration. Compositions comprising a compound of the invention formulated in a compatible pharmaceutical carrier may also be prepared, placed in an appropriate container, and labeled for treatment of an indicated condition.

4.13 ANTIBODIES

Also included in the invention are antibodies to proteins, or fragments of proteins of the invention. The term "antibody" as used herein refers to immunoglobulin molecules and immunologically active portions of immunoglobulin (Ig) molecules, *i.e.*, molecules that contain an antigen-binding site that specifically binds (immunoreacts with) an antigen. Such antibodies include, but are not limited to, polyclonal, monoclonal, chimeric, single chain, F_{ab}, $F_{ab'}$ and $F_{(ab')2}$ fragments, and an F_{ab} expression library. In general, an antibody molecule obtained from humans relates to any of the classes IgG, IgM, IgA, IgE and IgD, which differ from one another by the nature of the heavy chain present in the molecule. Certain classes have subclasses as well, such as IgG_1, IgG_2, and others. Furthermore, in humans, the light chain may be a kappa chain or a lambda chain. Reference herein to antibodies includes a reference to all such classes, subclasses and types of human antibody species.

An isolated related protein of the invention may be intended to serve as an antigen, or a portion or fragment thereof, and additionally can be used as an immunogen to generate antibodies that immunospecifically bind the antigen, using standard techniques for polyclonal and monoclonal antibody preparation. The full-length protein can be used or, alternatively, the invention provides antigenic peptide fragments of the antigen for use as immunogens. An antigenic peptide fragment comprises at least 6 amino acid residues of the amino acid sequence of the full length protein, (for example the amino acid sequence shown in SEQ ID NO: 30369), and encompasses an epitope thereof such that an antibody raised against the peptide forms a specific immune complex with the full length protein or with any fragment that contains the epitope. Preferably, the antigenic peptide comprises at least 10 amino acid residues, or at least 15 amino acid residues, or at least 20 amino acid residues, or at least 30 amino acid residues. Preferred epitopes encompassed by the antigenic peptide are regions of the protein that are located on its surface; commonly these are hydrophilic regions.

In certain embodiments of the invention, at least one epitope encompassed by the antigenic peptide is a region on the surface of the protein of the invention that is located on the

surface of the protein, *e.g.*, a hydrophilic region. A hydrophobicity analysis of the human related protein sequence will indicate which regions of a related protein are particularly hydrophilic and, therefore, are likely to encode surface residues useful for targeting antibody production. As a means for targeting antibody production, hydropathy plots showing regions of hydrophilicity and hydrophobicity may be generated by any method well known in the art, including, for example, the Kyte Doolittle or the Hopp Woods methods, either with or without Fourier transformation. See, *e.g.*, Hopp and Woods, 1981, *Proc. Nat. Acad. Sci. USA* 78: 3824-3828; Kyte and Doolittle 1982, *J. Mol. Biol.* 157: 105-142, each of which is incorporated herein by reference in its entirety. Antibodies that are specific for one or more domains within an antigenic protein, or derivatives, fragments, analogs or homologs thereof, are also provided herein.

A protein of the invention, or a derivative, fragment, analog, homolog or ortholog thereof, may be utilized as an immunogen in the generation of antibodies that immunospecifically bind these protein components.

Various procedures known within the art may be used for the production of polyclonal or monoclonal antibodies directed against a protein of the invention, or against derivatives, fragments, analogs homologs or orthologs thereof (see, for example, Antibodies: A Laboratory Manual, Harlow E, and Lane D, 1988, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, incorporated herein by reference). Some of these antibodies are discussed below.

5.13.1 Polyclonal Antibodies

For the production of polyclonal antibodies, various suitable host animals (*e.g.*, rabbit, goat, mouse or other mammal) may be immunized by one or more injections with the native protein, a synthetic variant thereof, or a derivative of the foregoing. An appropriate immunogenic preparation can contain, for example, the naturally occurring immunogenic protein, a chemically synthesized polypeptide representing the immunogenic protein, or a recombinantly expressed immunogenic protein. Furthermore, the protein may be conjugated to a second protein known to be immunogenic in the mammal being immunized. Examples of such immunogenic proteins include but are not limited to keyhole limpet hemocyanin, serum albumin, bovine thyroglobulin, and soybean trypsin inhibitor. The preparation can further include an adjuvant. Various adjuvants used to increase the immunological response include, but are not limited to, Freund's (complete and incomplete), mineral gels (*e.g.*, aluminum hydroxide), surface active substances (*e.g.*, lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, dinitrophenol, etc.), adjuvants usable in humans such as Bacille Calmette-Guerin and Corynebacterium parvum, or similar immunostimulatory agents. Additional examples of

adjuvants which can be employed include MPL-TDM adjuvant (monophosphoryl Lipid A, synthetic trehalose dicorynomycolate).

The polyclonal antibody molecules directed against the immunogenic protein can be isolated from the mammal (*e.g.*, from the blood) and further purified by well known techniques, such as affinity chromatography using protein A or protein G, which provide primarily the IgG fraction of immune serum. Subsequently, or alternatively, the specific antigen which is the target of the immunoglobulin sought, or an epitope thereof, may be immobilized on a column to purify the immune specific antibody by immunoaffinity chromatography. Purification of immunoglobulins is discussed, for example, by D. Wilkinson (The Scientist, published by The Scientist, Inc., Philadelphia PA, Vol. 14, No. 8 (April 17, 2000), pp. 25-28).

5.13.2 Monoclonal Antibodies

The term "monoclonal antibody" (MAb) or "monoclonal antibody composition", as used herein, refers to a population of antibody molecules that contain only one molecular species of antibody molecule consisting of a unique light chain gene product and a unique heavy chain gene product. In particular, the complementarity determining regions (CDRs) of the monoclonal antibody are identical in all the molecules of the population. MAbs thus contain an antigen-binding site capable of immunoreacting with a particular epitope of the antigen characterized by a unique binding affinity for it.

Monoclonal antibodies can be prepared using hybridoma methods, such as those described by Kohler and Milstein, Nature, 256:495 (1975). In a hybridoma method, a mouse, hamster, or other appropriate host animal, is typically immunized with an immunizing agent to elicit lymphocytes that produce or are capable of producing antibodies that will specifically bind to the immunizing agent. Alternatively, the lymphocytes can be immunized in vitro.

The immunizing agent will typically include the protein antigen, a fragment thereof or a fusion protein thereof. Generally, either peripheral blood lymphocytes are used if cells of human origin are desired, or spleen cells or lymph node cells are used if non-human mammalian sources are desired. The lymphocytes are then fused with an immortalized cell line using a suitable fusing agent, such as polyethylene glycol, to form a hybridoma cell (Goding, Monoclonal Antibodies: Principles and Practice, Academic Press, (1986) pp. 59-103). Immortalized cell lines are usually transformed mammalian cells, particularly myeloma cells of rodent, bovine and human origin. Usually, rat or mouse myeloma cell lines are employed. The hybridoma cells can be cultured in a suitable culture medium that preferably contains one or more substances that inhibit the growth or survival of the unfused, immortalized cells. For example, if the parental cells lack the enzyme hypoxanthine guanine phosphoribosyl transferase (HGPRT or HPRT), the

culture medium for the hybridomas typically will include hypoxanthine, aminopterin, and thymidine ("HAT medium"), which substances prevent the growth of HGPRT-deficient cells.

Preferred immortalized cell lines are those that fuse efficiently, support stable high level expression of antibody by the selected antibody-producing cells, and are sensitive to a medium such as HAT medium. More preferred immortalized cell lines are murine myeloma lines, which can be obtained, for instance, from the Salk Institute Cell Distribution Center, San Diego, California and the American Type Culture Collection, Manassas, Virginia. Human myeloma and mouse-human heteromyeloma cell lines also have been described for the production of human monoclonal antibodies (Kozbor, J. Immunol., 133:3001 (1984); Brodeur et al., Monoclonal Antibody Production Techniques and Applications, Marcel Dekker, Inc., New York, (1987) pp. 51-63).

The culture medium in which the hybridoma cells are cultured can then be assayed for the presence of monoclonal antibodies directed against the antigen. Preferably, the binding specificity of monoclonal antibodies produced by the hybridoma cells is determined by immunoprecipitation or by an in vitro binding assay, such as radioimmunoassay (RIA) or enzyme-linked immunoabsorbent assay (ELISA). Such techniques and assays are known in the art. The binding affinity of the monoclonal antibody can, for example, be determined by the Scatchard analysis of Munson and Pollard, Anal. Biochem., 107:220 (1980). Preferably, antibodies having a high degree of specificity and a high binding affinity for the target antigen are isolated.

After the desired hybridoma cells are identified, the clones can be subcloned by limiting dilution procedures and grown by standard methods. Suitable culture media for this purpose include, for example, Dulbecco's Modified Eagle's Medium and RPMI-1640 medium. Alternatively, the hybridoma cells can be grown in vivo as ascites in a mammal.

The monoclonal antibodies secreted by the subclones can be isolated or purified from the culture medium or ascites fluid by conventional immunoglobulin purification procedures such as, for example, protein A-Sepharose, hydroxylapatite chromatography, gel electrophoresis, dialysis, or affinity chromatography.

The monoclonal antibodies can also be made by recombinant DNA methods, such as those described in U.S. Patent No. 4,816,567. DNA encoding the monoclonal antibodies of the invention can be readily isolated and sequenced using conventional procedures (*e.g.*, by using oligonucleotide probes that are capable of binding specifically to genes encoding the heavy and light chains of murine antibodies). The hybridoma cells of the invention serve as a preferred source of such DNA. Once isolated, the DNA can be placed into expression vectors, which are then transfected into host cells such as simian COS cells, Chinese hamster ovary (CHO) cells, or

myeloma cells that do not otherwise produce immunoglobulin protein, to obtain the synthesis of monoclonal antibodies in the recombinant host cells. The DNA also can be modified, for example, by substituting the coding sequence for human heavy and light chain constant domains in place of the homologous murine sequences (U.S. Patent No. 4,816,567; Morrison, Nature 368, 812-13 (1994)) or by covalently joining to the immunoglobulin coding sequence all or part of the coding sequence for a non-immunoglobulin polypeptide. Such a non-immunoglobulin polypeptide can be substituted for the constant domains of an antibody of the invention, or can be substituted for the variable domains of one antigen-combining site of an antibody of the invention to create a chimeric bivalent antibody.

5.13.2 Humanized Antibodies

The antibodies directed against the protein antigens of the invention can further comprise humanized antibodies or human antibodies. These antibodies are suitable for administration to humans without engendering an immune response by the human against the administered immunoglobulin. Humanized forms of antibodies are chimeric immunoglobulins, immunoglobulin chains or fragments thereof (such as Fv, Fab, Fab', $F(ab')_2$ or other antigen-binding subsequences of antibodies) that are principally comprised of the sequence of a human immunoglobulin, and contain minimal sequence derived from a non-human immunoglobulin. Humanization can be performed following the method of Winter and co-workers (Jones et al., Nature, 321:522-525 (1986); Riechmann et al., Nature, 332:323-327 (1988); Verhoeyen et al., Science, 239:1534-1536 (1988)), by substituting rodent CDRs or CDR sequences for the corresponding sequences of a human antibody. (See also U.S. Patent No. 5,225,539.) In some instances, Fv framework residues of the human immunoglobulin are replaced by corresponding non-human residues. Humanized antibodies can also comprise residues which are found neither in the recipient antibody nor in the imported CDR or framework sequences. In general, the humanized antibody will comprise substantially all of at least one, and typically two, variable domains, in which all or substantially all of the CDR regions correspond to those of a non-human immunoglobulin and all or substantially all of the framework regions are those of a human immunoglobulin consensus sequence. The humanized antibody optimally also will comprise at least a portion of an immunoglobulin constant region (Fc), typically that of a human immunoglobulin (Jones et al., 1986; Riechmann et al., 1988; and Presta, Curr. Op. Struct. Biol., 2:593-596 (1992)).

5.13.3 Human Antibodies

Fully human antibodies relate to antibody molecules in which essentially the entire sequences of both the light chain and the heavy chain, including the CDRs, arise from human genes. Such antibodies are termed "human antibodies", or "fully human antibodies" herein. Human monoclonal antibodies can be prepared by the trioma technique; the human B-cell hybridoma technique (see Kozbor, et al., 1983 Immunol Today 4: 72) and the EBV hybridoma technique to produce human monoclonal antibodies (see Cole, et al., 1985 In: MONOCLONAL ANTIBODIES AND CANCER THERAPY, Alan R. Liss, Inc., pp. 77-96). Human monoclonal antibodies may be utilized in the practice of the present invention and may be produced by using human hybridomas (see Cote, et al., 1983. Proc Natl Acad Sci USA 80: 2026-2030) or by transforming human B-cells with Epstein Barr Virus in vitro (see Cole, et al., 1985 In: MONOCLONAL ANTIBODIES AND CANCER THERAPY, Alan R. Liss, Inc., pp. 77-96).

In addition, human antibodies can also be produced using additional techniques, including phage display libraries (Hoogenboom and Winter, J. Mol. Biol., 227:381 (1991); Marks et al., J. Mol. Biol., 222:581 (1991)). Similarly, human antibodies can be made by introducing human immunoglobulin loci into transgenic animals, *e.g.*, mice in which the endogenous immunoglobulin genes have been partially or completely inactivated. Upon challenge, human antibody production is observed, which closely resembles that seen in humans in all respects, including gene rearrangement, assembly, and antibody repertoire. This approach is described, for example, in U.S. Patent Nos. 5,545,807; 5,545,806; 5,569,825; 5,625,126; 5,633,425; 5,661,016, and in Marks et al. (Bio/Technology 10, 779-783 (1992)); Lonberg et al. (Nature 368 856-859 (1994)); Morrison (Nature 368, 812-13 (1994)); Fishwild et al,(Nature Biotechnology 14, 845-51 (1996)); Neuberger (Nature Biotechnology 14, 826 (1996)); and Lonberg and Huszar (Intern. Rev. Immunol. 13 65-93 (1995)).

Human antibodies may additionally be produced using transgenic nonhuman animals which are modified so as to produce fully human antibodies rather than the animal's endogenous antibodies in response to challenge by an antigen. (See PCT publication WO94/02602). The endogenous genes encoding the heavy and light immunoglobulin chains in the nonhuman host have been incapacitated, and active loci encoding human heavy and light chain immunoglobulins are inserted into the host's genome. The human genes are incorporated, for example, using yeast artificial chromosomes containing the requisite human DNA segments. An animal which provides all the desired modifications is then obtained as progeny by crossbreeding intermediate transgenic animals containing fewer than the full complement of the modifications. The preferred embodiment of such a nonhuman animal is a mouse, and is termed the Xenomouse™ as disclosed in PCT publications WO 96/33735 and WO 96/34096. This animal produces B cells which secrete fully human immunoglobulins. The antibodies can be obtained directly from

the animal after immunization with an immunogen of interest, as, for example, a preparation of a polyclonal antibody, or alternatively from immortalized B cells derived from the animal, such as hybridomas producing monoclonal antibodies. Additionally, the genes encoding the immunoglobulins with human variable regions can be recovered and expressed to obtain the antibodies directly, or can be further modified to obtain analogs of antibodies such as, for example, single chain Fv molecules.

An example of a method of producing a nonhuman host, exemplified as a mouse, lacking expression of an endogenous immunoglobulin heavy chain is disclosed in U.S. Patent No. 5,939,598. It can be obtained by a method including deleting the J segment genes from at least one endogenous heavy chain locus in an embryonic stem cell to prevent rearrangement of the locus and to prevent formation of a transcript of a rearranged immunoglobulin heavy chain locus, the deletion being effected by a targeting vector containing a gene encoding a selectable marker; and producing from the embryonic stem cell a transgenic mouse whose somatic and germ cells contain the gene encoding the selectable marker.

A method for producing an antibody of interest, such as a human antibody, is disclosed in U.S. Patent No. 5,916,771. It includes introducing an expression vector that contains a nucleotide sequence encoding a heavy chain into one mammalian host cell in culture, introducing an expression vector containing a nucleotide sequence encoding a light chain into another mammalian host cell, and fusing the two cells to form a hybrid cell. The hybrid cell expresses an antibody containing the heavy chain and the light chain.

In a further improvement on this procedure, a method for identifying a clinically relevant epitope on an immunogen, and a correlative method for selecting an antibody that binds immunospecifically to the relevant epitope with high affinity, are disclosed in PCT publication WO 99/53049.

5.13.4 F_{ab} Fragments and Single Chain Antibodies

According to the invention, techniques can be adapted for the production of single-chain antibodies specific to an antigenic protein of the invention (see *e.g.*, U.S. Patent No. 4,946,778). In addition, methods can be adapted for the construction of F_{ab} expression libraries (see *e.g.*, Huse, et al., 1989 Science 246: 1275-1281) to allow rapid and effective identification of monoclonal F_{ab} fragments with the desired specificity for a protein or derivatives, fragments, analogs or homologs thereof. Antibody fragments that contain the idiotypes to a protein antigen may be produced by techniques known in the art including, but not limited to: (i) an $F_{(ab')2}$ fragment produced by pepsin digestion of an antibody molecule; (ii) an F_{ab} fragment generated

by reducing the disulfide bridges of an $F_{(ab')2}$ fragment; (iii) an F_{ab} fragment generated by the treatment of the antibody molecule with papain and a reducing agent and (iv) F_v fragments.

5.13.5 Bispecific Antibodies

Bispecific antibodies are monoclonal, preferably human or humanized, antibodies that have binding specificities for at least two different antigens. In the present case, one of the binding specificities is for an antigenic protein of the invention. The second binding target is any other antigen, and advantageously is a cell-surface protein or receptor or receptor subunit.

Methods for making bispecific antibodies are known in the art. Traditionally, the recombinant production of bispecific antibodies is based on the co-expression of two immunoglobulin heavy-chain/light-chain pairs, where the two heavy chains have different specificities (Milstein and Cuello, Nature, 305:537-539 (1983)). Because of the random assortment of immunoglobulin heavy and light chains, these hybridomas (quadromas) produce a potential mixture of ten different antibody molecules, of which only one has the correct bispecific structure. The purification of the correct molecule is usually accomplished by affinity chromatography steps. Similar procedures are disclosed in WO 93/08829, published 13 May 1993, and in Traunecker *et al.*, 1991 *EMBO J.*, 10:3655-3659.

Antibody variable domains with the desired binding specificities (antibody-antigen combining sites) can be fused to immunoglobulin constant domain sequences. The fusion preferably is with an immunoglobulin heavy-chain constant domain, comprising at least part of the hinge, CH2, and CH3 regions. It is preferred to have the first heavy-chain constant region (CH1) containing the site necessary for light-chain binding present in at least one of the fusions. DNAs encoding the immunoglobulin heavy-chain fusions and, if desired, the immunoglobulin light chain, are inserted into separate expression vectors, and are co-transfected into a suitable host organism. For further details of generating bispecific antibodies see, for example, Suresh et al., Methods in Enzymology, 121:210 (1986).

According to another approach described in WO 96/27011, the interface between a pair of antibody molecules can be engineered to maximize the percentage of heterodimers which are recovered from recombinant cell culture. The preferred interface comprises at least a part of the CH3 region of an antibody constant domain. In this method, one or more small amino acid side chains from the interface of the first antibody molecule are replaced with larger side chains (*e.g.* tyrosine or tryptophan). Compensatory "cavities" of identical or similar size to the large side chain(s) are created on the interface of the second antibody molecule by replacing large amino acid side chains with smaller ones (*e.g.* alanine or threonine). This provides a mechanism for increasing the yield of the heterodimer over other unwanted end-products such as homodimers.

Bispecific antibodies can be prepared as full length antibodies or antibody fragments (*e.g.* $F(ab')_2$ bispecific antibodies). Techniques for generating bispecific antibodies from antibody fragments have been described in the literature. For example, bispecific antibodies can be prepared using chemical linkage. Brennan et al., Science 229:81 (1985) describe a procedure wherein intact antibodies are proteolytically cleaved to generate $F(ab')_2$ fragments. These fragments are reduced in the presence of the dithiol complexing agent sodium arsenite to stabilize vicinal dithiols and prevent intermolecular disulfide formation. The Fab' fragments generated are then converted to thionitrobenzoate (TNB) derivatives. One of the Fab'-TNB derivatives is then reconverted to the Fab'-thiol by reduction with mercaptoethylamine and is mixed with an equimolar amount of the other Fab'-TNB derivative to form the bispecific antibody. The bispecific antibodies produced can be used as agents for the selective immobilization of enzymes.

Additionally, Fab' fragments can be directly recovered from E. coli and chemically coupled to form bispecific antibodies. Shalaby et al., J. Exp. Med. 175:217-225 (1992) describe the production of a fully humanized bispecific antibody $F(ab')_2$ molecule. Each Fab' fragment was separately secreted from E. coli and subjected to directed chemical coupling in vitro to form the bispecific antibody. The bispecific antibody thus formed was able to bind to cells overexpressing the ErbB2 receptor and normal human T cells, as well as trigger the lytic activity of human cytotoxic lymphocytes against human breast tumor targets.

Various techniques for making and isolating bispecific antibody fragments directly from recombinant cell culture have also been described. For example, bispecific antibodies have been produced using leucine zippers. Kostelny et al., J. Immunol. 148(5):1547-1553 (1992). The leucine zipper peptides from the Fos and Jun proteins were linked to the Fab' portions of two different antibodies by gene fusion. The antibody homodimers were reduced at the hinge region to form monomers and then re-oxidized to form the antibody heterodimers. This method can also be utilized for the production of antibody homodimers. The "diabody" technology described by Hollinger et al., Proc. Natl. Acad. Sci. USA 90:6444-6448 (1993) has provided an alternative mechanism for making bispecific antibody fragments. The fragments comprise a heavy-chain variable domain (V_H) connected to a light-chain variable domain (V_L) by a linker which is too short to allow pairing between the two domains on the same chain. Accordingly, the V_H and V_L domains of one fragment are forced to pair with the complementary V_L and V_H domains of another fragment, thereby forming two antigen-binding sites. Another strategy for making bispecific antibody fragments by the use of single-chain Fv (sFv) dimers has also been reported. See, Gruber et al., J. Immunol. 152:5368 (1994).

Antibodies with more than two valencies are contemplated. For example, trispecific antibodies can be prepared. Tutt et al., J. Immunol. 147:60 (1991).

Exemplary bispecific antibodies can bind to two different epitopes, at least one of which originates in the protein antigen of the invention. Alternatively, an anti-antigenic arm of an immunoglobulin molecule can be combined with an arm which binds to a triggering molecule on a leukocyte such as a T-cell receptor molecule (*e.g.* CD2, CD3, CD28, or B7), or Fc receptors for IgG (FcγR), such as FcγRI (CD64), FcγRII (CD32) and FcγRIII (CD16) so as to focus cellular defense mechanisms to the cell expressing the particular antigen. Bispecific antibodies can also be used to direct cytotoxic agents to cells which express a particular antigen. These antibodies possess an antigen-binding arm and an arm which binds a cytotoxic agent or a radionuclide chelator, such as EOTUBE, DPTA, DOTA, or TETA. Another bispecific antibody of interest binds the protein antigen described herein and further binds tissue factor (TF).

5.13.6 Heteroconjugate Antibodies

Heteroconjugate antibodies are also within the scope of the present invention. Heteroconjugate antibodies are composed of two covalently joined antibodies. Such antibodies have, for example, been proposed to target immune system cells to unwanted cells (U.S. Patent No. 4,676,980), and for treatment of HIV infection (WO 91/00360; WO 92/200373; EP 03089). It is contemplated that the antibodies can be prepared in vitro using known methods in synthetic protein chemistry, including those involving crosslinking agents. For example, immunotoxins can be constructed using a disulfide exchange reaction or by forming a thioether bond. Examples of suitable reagents for this purpose include iminothiolate and methyl-4-mercaptobutyrimidate and those disclosed, for example, in U.S. Patent No. 4,676,980.

5.13.7 Effector Function Engineering

It can be desirable to modify the antibody of the invention with respect to effector function, so as to enhance, *e.g.*, the effectiveness of the antibody in treating cancer. For example, cysteine residue(s) can be introduced into the Fc region, thereby allowing interchain disulfide bond formation in this region. The homodimeric antibody thus generated can have improved internalization capability and/or increased complement-mediated cell killing and antibody-dependent cellular cytotoxicity (ADCC). See Caron et al., J. Exp Med., 176: 1191-1195 (1992) and Shopes, J. Immunol., 148: 2918-2922 (1992). Homodimeric antibodies with enhanced anti-tumor activity can also be prepared using heterobifunctional cross-linkers as described in Wolff et al. Cancer Research, 53: 2560-2565 (1993). Alternatively, an antibody can

be engineered that has dual Fc regions and can thereby have enhanced complement lysis and ADCC capabilities. See Stevenson et al., Anti-Cancer Drug Design, 3: 219-230 (1989).

5.13.8 Immunoconjugates

The invention also pertains to immunoconjugates comprising an antibody conjugated to a cytotoxic agent such as a chemotherapeutic agent, toxin (*e.g.*, an enzymatically active toxin of bacterial, fungal, plant, or animal origin, or fragments thereof), or a radioactive isotope (*i.e.*, a radioconjugate).

Chemotherapeutic agents useful in the generation of such immunoconjugates have been described above. Enzymatically active toxins and fragments thereof that can be used include diphtheria A chain, nonbinding active fragments of diphtheria toxin, exotoxin A chain (from Pseudomonas aeruginosa), ricin A chain, abrin A chain, modeccin A chain, alpha-sarcin, Aleurites fordii proteins, dianthin proteins, Phytolaca americana proteins (PAPI, PAPII, and PAP-S), momordica charantia inhibitor, curcin, crotin, sapaonaria officinalis inhibitor, gelonin, mitogellin, restrictocin, phenomycin, enomycin, and the tricothecenes. A variety of radionuclides are available for the production of radioconjugated antibodies. Examples include ^{212}Bi, ^{131}I, ^{131}In, ^{90}Y, and ^{186}Re.

Conjugates of the antibody and cytotoxic agent are made using a variety of bifunctional protein-coupling agents such as N-succinimidyl-3-(2-pyridyldithiol) propionate (SPDP), iminothiolane (IT), bifunctional derivatives of imidoesters (such as dimethyl adipimidate HCL), active esters (such as disuccinimidyl suberate), aldehydes (such as glutareldehyde), bis-azido compounds (such as bis (p-azidobenzoyl) hexanediamine), bis-diazonium derivatives (such as bis-(p-diazoniumbenzoyl)-ethylenediamine), diisocyanates (such as tolyene 2,6-diisocyanate), and bis-active fluorine compounds (such as 1,5-difluoro-2,4-dinitrobenzene). For example, a ricin immunotoxin can be prepared as described in Vitetta et al., Science, 238: 1098 (1987). Carbon-14-labeled 1-isothiocyanatobenzyl-3-methyldiethylene triaminepentaacetic acid (MX-DTPA) is an exemplary chelating agent for conjugation of radionucleotide to the antibody. See WO94/11026.

In another embodiment, the antibody can be conjugated to a "receptor" (such streptavidin) for utilization in tumor pretargeting wherein the antibody-receptor conjugate is administered to the patient, followed by removal of unbound conjugate from the circulation using a clearing agent and then administration of a "ligand" (*e.g.*, avidin) that is in turn conjugated to a cytotoxic agent.

4.14 COMPUTER READABLE SEQUENCES

In one application of this embodiment, a nucleotide sequence of the present invention can be recorded on computer readable media. As used herein, "computer readable media" refers to any medium which can be read and accessed directly by a computer. Such media include, but are not limited to: magnetic storage media, such as floppy discs, hard disc storage medium, and magnetic tape; optical storage media such as CD-ROM; electrical storage media such as RAM and ROM; and hybrids of these categories such as magnetic/optical storage media. A skilled artisan can readily appreciate how any of the presently known computer readable mediums can be used to create a manufacture comprising computer readable medium having recorded thereon a nucleotide sequence of the present invention. As used herein, "recorded" refers to a process for storing information on computer readable medium. A skilled artisan can readily adopt any of the presently known methods for recording information on computer readable medium to generate manufactures comprising the nucleotide sequence information of the present invention.

A variety of data storage structures are available to a skilled artisan for creating a computer readable medium having recorded thereon a nucleotide sequence of the present invention. The choice of the data storage structure will generally be based on the means chosen to access the stored information. In addition, a variety of data processor programs and formats can be used to store the nucleotide sequence information of the present invention on computer readable medium. The sequence information can be represented in a word processing text file, formatted in commercially-available software such as WordPerfect and Microsoft Word, or represented in the form of an ASCII file, stored in a database application, such as DB2, Sybase, Oracle, or the like. A skilled artisan can readily adapt any number of data processor structuring formats (*e.g.* text file or database) in order to obtain computer readable medium having recorded thereon the nucleotide sequence information of the present invention.

By providing any of the nucleotide sequences SEQ ID NO: 1-30368 or a representative fragment thereof; or a nucleotide sequence at least 95% identical to any of the nucleotide sequences of SEQ ID NO: 1-30368 in computer readable form, a skilled artisan can routinely access the sequence information for a variety of purposes. Computer software is publicly available which allows a skilled artisan to access sequence information provided in a computer readable medium. The examples which follow demonstrate how software which implements the BLAST (Altschul et al., J. Mol. Biol. 215:403-410 (1990)) and BLAZE (Brutlag et al., Comp. Chem. 17:203-207 (1993)) search algorithms on a Sybase system is used to identify open reading frames (ORFs) within a nucleic acid sequence. Such ORFs may be protein encoding fragments and may be useful in producing commercially important proteins such as enzymes used in fermentation reactions and in the production of commercially useful metabolites.

As used herein, "a computer-based system" refers to the hardware means, software means, and data storage means used to analyze the nucleotide sequence information of the present invention. The minimum hardware means of the computer-based systems of the present invention comprises a central processing unit (CPU), input means, output means, and data storage means. A skilled artisan can readily appreciate that any one of the currently available computer-based systems are suitable for use in the present invention. As stated above, the computer-based systems of the present invention comprise a data storage means having stored therein a nucleotide sequence of the present invention and the necessary hardware means and software means for supporting and implementing a search means. As used herein, "data storage means" refers to memory which can store nucleotide sequence information of the present invention, or a memory access means which can access manufactures having recorded thereon the nucleotide sequence information of the present invention.

As used herein, "search means" refers to one or more programs which are implemented on the computer-based system to compare a target sequence or target structural motif with the sequence information stored within the data storage means. Search means are used to identify fragments or regions of a known sequence which match a particular target sequence or target motif. A variety of known algorithms are disclosed publicly and a variety of commercially available software for conducting search means are and can be used in the computer-based systems of the present invention. Examples of such software includes, but is not limited to, Smith-Waterman, MacPattern (EMBL), BLASTN and BLASTA (NPOLYPEPTIDEIA). A skilled artisan can readily recognize that any one of the available algorithms or implementing software packages for conducting homology searches can be adapted for use in the present computer-based systems. As used herein, a "target sequence" can be any nucleic acid or amino acid sequence of six or more nucleotides or two or more amino acids. A skilled artisan can readily recognize that the longer a target sequence is, the less likely a target sequence will be present as a random occurrence in the database. The most preferred sequence length of a target sequence is from about 10 to 300 amino acids, more preferably from about 30 to 100 nucleotide residues. However, it is well recognized that searches for commercially important fragments, such as sequence fragments involved in gene expression and protein processing, may be of shorter length.

As used herein, "a target structural motif," or "target motif," refers to any rationally selected sequence or combination of sequences in which the sequence(s) are chosen based on a three-dimensional configuration which is formed upon the folding of the target motif. There are a variety of target motifs known in the art. Protein target motifs include, but are not limited to, enzyme active sites and signal sequences. Nucleic acid target motifs include, but are not limited

to, promoter sequences, hairpin structures and inducible expression elements (protein binding sequences).

4.15 TRIPLE HELIX FORMATION

In addition, the fragments of the present invention, as broadly described, can be used to control gene expression through triple helix formation or antisense DNA or RNA, both of which methods are based on the binding of a polynucleotide sequence to DNA or RNA. Polynucleotides suitable for use in these methods are preferably 20 to 40 bases in length and are designed to be complementary to a region of the gene involved in transcription (triple helix - see Lee et al., Nucl. Acids Res. 6:3073 (1979); Cooney et al., Science 15241:456 (1988); and Dervan et al., Science 251:1360 (1991)) or to the mRNA itself (antisense - Olmno, J. Neurochem. 56:560 (1991); Oligodeoxynucleotides as Antisense Inhibitors of Gene Expression, CRC Press, Boca Raton, FL (1988)). Triple helix-formation optimally results in a shut-off of RNA transcription from DNA, while antisense RNA hybridization blocks translation of an mRNA molecule into polypeptide. Both techniques have been demonstrated to be effective in model systems. Information contained in the sequences of the present invention is necessary for the design of an antisense or triple helix oligonucleotide.

4.16 DIAGNOSTIC ASSAYS AND KITS

The present invention further provides methods to identify the presence or expression of one of the ORFs of the present invention, or homolog thereof, in a test sample, using a nucleic acid probe or antibodies of the present invention, optionally conjugated or otherwise associated with a suitable label.

In general, methods for detecting a polynucleotide of the invention can comprise contacting a sample with a compound that binds to and forms a complex with the polynucleotide for a period sufficient to form the complex, and detecting the complex, so that if a complex is detected, a polynucleotide of the invention is detected in the sample. Such methods can also comprise contacting a sample under stringent hybridization conditions with nucleic acid primers that anneal to a polynucleotide of the invention under such conditions, and amplifying annealed polynucleotides, so that if a polynucleotide is amplified, a polynucleotide of the invention is detected in the sample.

In general, methods for detecting a polypeptide of the invention can comprise contacting a sample with a compound that binds to and forms a complex with the polypeptide for a period sufficient to form the complex, and detecting the complex, so that if a complex is detected, a polypeptide of the invention is detected in the sample.

In detail, such methods comprise incubating a test sample with one or more of the antibodies or one or more of the nucleic acid probes of the present invention and assaying for binding of the nucleic acid probes or antibodies to components within the test sample.

Conditions for incubating a nucleic acid probe or antibody with a test sample vary. Incubation conditions depend on the format employed in the assay, the detection methods employed, and the type and nature of the nucleic acid probe or antibody used in the assay. One skilled in the art will recognize that any one of the commonly available hybridization, amplification or immunological assay formats can readily be adapted to employ the nucleic acid probes or antibodies of the present invention. Examples of such assays can be found in Chard, T., An Introduction to Radioimmunoassay and Related Techniques, Elsevier Science Publishers, Amsterdam, The Netherlands (1986); Bullock, G.R. et al., Techniques in Immunocytochemistry, Academic Press, Orlando, FL Vol. 1 (1982), Vol. 2 (1983), Vol. 3 (1985); Tijssen, P., Practice and Theory of immunoassays: Laboratory Techniques in Biochemistry and Molecular Biology, Elsevier Science Publishers, Amsterdam, The Netherlands (1985). The test samples of the present invention include cells, protein or membrane extracts of cells, or biological fluids such as sputum, blood, serum, plasma, or urine. The test sample used in the above-described method will vary based on the assay format, nature of the detection method and the tissues, cells or extracts used as the sample to be assayed. Methods for preparing protein extracts or membrane extracts of cells are well known in the art and can be readily be adapted in order to obtain a sample which is compatible with the system utilized.

In another embodiment of the present invention, kits are provided which contain the necessary reagents to carry out the assays of the present invention. Specifically, the invention provides a compartment kit to receive, in close confinement, one or more containers which comprises: (a) a first container comprising one of the probes or antibodies of the present invention; and (b) one or more other containers comprising one or more of the following: wash reagents, reagents capable of detecting presence of a bound probe or antibody.

In detail, a compartment kit includes any kit in which reagents are contained in separate containers. Such containers include small glass containers, plastic containers or strips of plastic or paper. Such containers allows one to efficiently transfer reagents from one compartment to another compartment such that the samples and reagents are not cross-contaminated, and the agents or solutions of each container can be added in a quantitative fashion from one compartment to another. Such containers will include a container which will accept the test sample, a container which contains the antibodies used in the assay, containers which contain wash reagents (such as phosphate buffered saline, Tris-buffers, etc.), and containers which contain the reagents used to detect the bound antibody or probe. Types of detection reagents

include labeled nucleic acid probes, labeled secondary antibodies, or in the alternative, if the primary antibody is labeled, the enzymatic, or antibody binding reagents which are capable of reacting with the labeled antibody. One skilled in the art will readily recognize that the disclosed probes and antibodies of the present invention can be readily incorporated into one of the established kit formats which are well known in the art.

4.17 MEDICAL IMAGING

The novel polypeptides and binding partners of the invention are useful in medical imaging of sites expressing the molecules of the invention (*e.g.*, where the polypeptide of the invention is involved in the immune response, for imaging sites of inflammation or infection). See, *e.g.*, Kunkel et al., U.S. Pat. NO. 5,413,778. Such methods involve chemical attachment of a labeling or imaging agent, administration of the labeled polypeptide to a subject in a pharmaceutically acceptable carrier, and imaging the labeled polypeptide *in vivo* at the target site.

4.18 SCREENING ASSAYS

Using the isolated proteins and polynucleotides of the invention, the present invention further provides methods of obtaining and identifying agents which bind to a polypeptide encoded by an ORF corresponding to any of the nucleotide sequences set forth in SEQ ID NO: 1-30368, or bind to a specific domain of the polypeptide encoded by the nucleic acid. In detail, said method comprises the steps of:

(a) contacting an agent with an isolated protein encoded by an ORF of the present invention, or nucleic acid of the invention; and

(b) determining whether the agent binds to said protein or said nucleic acid.

In general, therefore, such methods for identifying compounds that bind to a polynucleotide of the invention can comprise contacting a compound with a polynucleotide of the invention for a time sufficient to form a polynucleotide/compound complex, and detecting the complex, so that if a polynucleotide/compound complex is detected, a compound that binds to a polynucleotide of the invention is identified.

Likewise, in general, therefore, such methods for identifying compounds that bind to a polypeptide of the invention can comprise contacting a compound with a polypeptide of the invention for a time sufficient to form a polypeptide/compound complex, and detecting the complex, so that if a polypeptide/compound complex is detected, a compound that binds to a polynucleotide of the invention is identified.

Methods for identifying compounds that bind to a polypeptide of the invention can also comprise contacting a compound with a polypeptide of the invention in a cell for a time sufficient to form a polypeptide/compound complex, wherein the complex drives expression of a receptor gene sequence in the cell, and detecting the complex by detecting reporter gene sequence expression, so that if a polypeptide/compound complex is detected, a compound that binds a polypeptide of the invention is identified.

Compounds identified via such methods can include compounds which modulate the activity of a polypeptide of the invention (that is, increase or decrease its activity, relative to activity observed in the absence of the compound). Alternatively, compounds identified via such methods can include compounds which modulate the expression of a polynucleotide of the invention (that is, increase or decrease expression relative to expression levels observed in the absence of the compound). Compounds, such as compounds identified via the methods of the invention, can be tested using standard assays well known to those of skill in the art for their ability to modulate activity/expression.

The agents screened in the above assay can be, but are not limited to, peptides, carbohydrates, vitamin derivatives, or other pharmaceutical agents. The agents can be selected and screened at random or rationally selected or designed using protein modeling techniques.

For random screening, agents such as peptides, carbohydrates, pharmaceutical agents and the like are selected at random and are assayed for their ability to bind to the protein encoded by the ORF of the present invention. Alternatively, agents may be rationally selected or designed. As used herein, an agent is said to be "rationally selected or designed" when the agent is chosen based on the configuration of the particular protein. For example, one skilled in the art can readily adapt currently available procedures to generate peptides, pharmaceutical agents and the like, capable of binding to a specific peptide sequence, in order to generate rationally designed antipeptide peptides, for example see Hurby et al., Application of Synthetic Peptides: Antisense Peptides," In Synthetic Peptides, A User's Guide, W.H. Freeman, NY (1992), pp. 289-307, and Kaspczak et al., Biochemistry 28:9230-8 (1989), or pharmaceutical agents, or the like.

In addition to the foregoing, one class of agents of the present invention, as broadly described, can be used to control gene expression through binding to one of the ORFs or EMFs of the present invention. As described above, such agents can be randomly screened or rationally designed/selected. Targeting the ORF or EMF allows a skilled artisan to design sequence specific or element specific agents, modulating the expression of either a single ORF or multiple ORFs which rely on the same EMF for expression control. One class of DNA binding agents are agents which contain base residues which hybridize or form a triple helix formation by binding to DNA or RNA. Such agents can be based on the classic phosphodiester,

ribonucleic acid backbone, or can be a variety of sulfhydryl or polymeric derivatives which have base attachment capacity.

Agents suitable for use in these methods preferably contain 20 to 40 bases and are designed to be complementary to a region of the gene involved in transcription (triple helix - see Lee et al., Nucl. Acids Res. 6:3073 (1979); Cooney et al., Science 241:456 (1988); and Dervan et al., Science 251:1360 (1991)) or to the mRNA itself (antisense - Okano, J. Neurochem. 56:560 (1991); Oligodeoxynucleotides as Antisense Inhibitors of Gene Expression, CRC Press, Boca Raton, FL (1988)). Triple helix-formation optimally results in a shut-off of RNA transcription from DNA, while antisense RNA hybridization blocks translation of an mRNA molecule into polypeptide. Both techniques have been demonstrated to be effective in model systems. Information contained in the sequences of the present invention is necessary for the design of an antisense or triple helix oligonucleotide and other DNA binding agents.

Agents that bind to a protein encoded by one of the ORFs of the present invention can be used as a diagnostic agent. Agents which bind to a protein encoded by one of the ORFs of the present invention can be formulated using known techniques to generate a pharmaceutical composition.

4.19 USE OF NUCLEIC ACIDS AS PROBES

Another aspect of the subject invention is to provide for polypeptide-specific nucleic acid hybridization probes capable of hybridizing with naturally occurring nucleotide sequences. The hybridization probes of the subject invention may be derived from any of the nucleotide sequences SEQ ID NO: 1-30368. Because the corresponding gene is only expressed in a limited number of tissues, a hybridization probe derived from of any of the nucleotide sequences SEQ ID NO: 1-30368 can be used as an indicator of the presence of RNA of cell type of such a tissue in a sample.

Any suitable hybridization technique can be employed, such as, for example, in situ hybridization. PCR as described in US Patents Nos. 4,683,195 and 4,965,188 provides additional uses for oligonucleotides based upon the nucleotide sequences. Such probes used in PCR may be of recombinant origin, may be chemically synthesized, or a mixture of both. The probe will comprise a discrete nucleotide sequence for the detection of identical sequences or a degenerate pool of possible sequences for identification of closely related genomic sequences.

Other means for producing specific hybridization probes for nucleic acids include the cloning of nucleic acid sequences into vectors for the production of mRNA probes. Such vectors are known in the art and are commercially available and may be used to synthesize RNA probes *in vitro* by means of the addition of the appropriate RNA polymerase as T7 or SP6 RNA

polymerase and the appropriate radioactively labeled nucleotides. The nucleotide sequences may be used to construct hybridization probes for mapping their respective genomic sequences. The nucleotide sequence provided herein may be mapped to a chromosome or specific regions of a chromosome using well known genetic and/or chromosomal mapping techniques. These techniques include in situ hybridization, linkage analysis against known chromosomal markers, hybridization screening with libraries or flow-sorted chromosomal preparations specific to known chromosomes, and the like. The technique of fluorescent in situ hybridization of chromosome spreads has been described, among other places, in Verma et al (1988) Human Chromosomes: A Manual of Basic Techniques, Pergamon Press, New York NY.

Fluorescent *in situ* hybridization of chromosomal preparations and other physical chromosome mapping techniques may be correlated with additional genetic map data. Examples of genetic map data can be found in the 1994 Genome Issue of Science (265:1981f). Correlation between the location of a nucleic acid on a physical chromosomal map and a specific disease (or predisposition to a specific disease) may help delimit the region of DNA associated with that genetic disease. The nucleotide sequences of the subject invention may be used to detect differences in gene sequences between normal, carrier or affected individuals.

4.20 PREPARATION OF SUPPORT BOUND OLIGONUCLEOTIDES

Oligonucleotides, *i.e.*, small nucleic acid segments, may be readily prepared by, for example, directly synthesizing the oligonucleotide by chemical means, as is commonly practiced using an automated oligonucleotide synthesizer.

Support bound oligonucleotides may be prepared by any of the methods known to those of skill in the art using any suitable support such as glass, polystyrene or Teflon. One strategy is to precisely spot oligonucleotides synthesized by standard synthesizers. Immobilization can be achieved using passive adsorption (Inouye & Hondo, (1990) J. Clin. Microbiol. 28(6) 1469-72); using UV light (Nagata *et al.*, 1985; Dahlen *et al.*, 1987; Morrissey & Collins, (1989) Mol. Cell Probes 3(2) 189-207) or by covalent binding of base modified DNA (Keller *et al.*, 1988; 1989); all references being specifically incorporated herein.

Another strategy that may be employed is the use of the strong biotin-streptavidin interaction as a linker. For example, Broude *et al.* (1994) Proc. Natl. Acad. Sci. USA 91(8) 3072-6, describe the use of biotinylated probes, although these are duplex probes, that are immobilized on streptavidin-coated magnetic beads. Streptavidin-coated beads may be purchased from Dynal, Oslo. Of course, this same linking chemistry is applicable to coating any surface with streptavidin. Biotinylated probes may be purchased from various sources, such as, *e.g.*, Operon Technologies (Alameda, CA).

Nunc Laboratories (Naperville, IL) is also selling suitable material that could be used. Nunc Laboratories have developed a method by which DNA can be covalently bound to the microwell surface termed Covalink NH. CovaLink NH is a polystyrene surface grafted with secondary amino groups (>NH) that serve as bridge-heads for further covalent coupling. CovaLink Modules may be purchased from Nunc Laboratories. DNA molecules may be bound to CovaLink exclusively at the 5'-end by a phosphoramidate bond, allowing immobilization of more than 1 pmol of DNA (Rasmussen *et al.*, (1991) Anal. Biochem. 198(1) 138-42).

The use of CovaLink NH strips for covalent binding of DNA molecules at the 5'-end has been described (Rasmussen et al., (1991). In this technology, a phosphoramidate bond is employed (Chu et al., (1983) Nucleic Acids Res. 11(8) 6513-29). This is beneficial as immobilization using only a single covalent bond is preferred. The phosphoramidate bond joins the DNA to the CovaLink NH secondary amino groups that are positioned at the end of spacer arms covalently grafted onto the polystyrene surface through a 2 nm long spacer arm. To link an oligonucleotide to CovaLink NH via an phosphoramidate bond, the oligonucleotide terminus must have a 5'-end phosphate group. It is, perhaps, even possible for biotin to be covalently bound to CovaLink and then streptavidin used to bind the probes.

More specifically, the linkage method includes dissolving DNA in water (7.5 ng/ul) and denaturing for 10 min. at 95°C and cooling on ice for 10 min. Ice-cold 0.1 M 1-methylimidazole, pH 7.0 (1-MeIm$_7$), is then added to a final concentration of 10 mM 1-MeIm$_7$. A ss DNA solution is then dispensed into CovaLink NH strips (75 ul/well) standing on ice.

Carbodiimide 0.2 M 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide (EDC), dissolved in 10 mM 1-MeIm$_7$, is made fresh and 25 ul added per well. The strips are incubated for 5 hours at 50°C. After incubation the strips are washed using, *e.g.*, Nunc-Immuno Wash; first the wells are washed 3 times, then they are soaked with washing solution for 5 min., and finally they are washed 3 times (where in the washing solution is 0.4 N NaOH, 0.25% SDS heated to 50°C).

It is contemplated that a further suitable method for use with the present invention is that described in PCT Patent Application WO 90/03382 (Southern & Maskos), incorporated herein by reference. This method of preparing an oligonucleotide bound to a support involves attaching a nucleoside 3'-reagent through the phosphate group by a covalent phosphodiester link to aliphatic hydroxyl groups carried by the support. The oligonucleotide is then synthesized on the supported nucleoside and protecting groups removed from the synthetic oligonucleotide chain under standard conditions that do not cleave the oligonucleotide from the support. Suitable reagents include nucleoside phosphoramidite and nucleoside hydrogen phosphorate.

An on-chip strategy for the preparation of DNA probe for the preparation of DNA probe arrays may be employed. For example, addressable laser-activated photodeprotection may be

employed in the chemical synthesis of oligonucleotides directly on a glass surface, as described by Fodor *et al.* (1991) Science 251(4995) 767-73, incorporated herein by reference. Probes may also be immobilized on nylon supports as described by Van Ness *et al.* (1991) Nucleic Acids Res. 19(12) 3345-50; or linked to Teflon using the method of Duncan & Cavalier (1988) Anal. Biochem. 169(1) 104-8; all references being specifically incorporated herein.

To link an oligonucleotide to a nylon support, as described by Van Ness *et al.* (1991), requires activation of the nylon surface via alkylation and selective activation of the 5'-amine of oligonucleotides with cyanuric chloride.

One particular way to prepare support bound oligonucleotides is to utilize the light-generated synthesis described by Pease *et al.*, (1994) PNAS USA 91(11) 5022-6, incorporated herein by reference). These authors used current photolithographic techniques to generate arrays of immobilized oligonucleotide probes (DNA chips). These methods, in which light is used to direct the synthesis of oligonucleotide probes in high-density, miniaturized arrays, utilize photolabile 5'-protected *N*-acyl-deoxynucleoside phosphoramidites, surface linker chemistry and versatile combinatorial synthesis strategies. A matrix of 256 spatially defined oligonucleotide probes may be generated in this manner.

4.21 PREPARATION OF NUCLEIC ACID FRAGMENTS

The nucleic acids may be obtained from any appropriate source, such as cDNAs, genomic DNA, chromosomal DNA, microdissected chromosome bands, cosmid or YAC inserts, and RNA, including mRNA without any amplification steps. For example, Sambrook *et al.* (1989) describes three protocols for the isolation of high molecular weight DNA from mammalian cells (p. 9.14-9.23).

DNA fragments may be prepared as clones in M13, plasmid or lambda vectors and/or prepared directly from genomic DNA or cDNA by PCR or other amplification methods. Samples may be prepared or dispensed in multiwell plates. About 100-1000 ng of DNA samples may be prepared in 2-500 ml of final volume.

The nucleic acids would then be fragmented by any of the methods known to those of skill in the art including, for example, using restriction enzymes as described at 9.24-9.28 of Sambrook *et al.* (1989), shearing by ultrasound and NaOH treatment.

Low pressure shearing is also appropriate, as described by Schriefer *et al.* (1990) Nucleic Acids Res. 18(24) 7455-6, incorporated herein by reference). In this method, DNA samples are passed through a small French pressure cell at a variety of low to intermediate pressures. A lever device allows controlled application of low to intermediate pressures to the cell. The results of

these studies indicate that low-pressure shearing is a useful alternative to sonic and enzymatic DNA fragmentation methods.

One particularly suitable way for fragmenting DNA is contemplated to be that using the two base recognition endonuclease, *Cvi*JI, described by Fitzgerald *et al.* (1992) Nucleic Acids Res. 20(14) 3753-62. These authors described an approach for the rapid fragmentation and fractionation of DNA into particular sizes that they contemplated to be suitable for shotgun cloning and sequencing.

The restriction endonuclease *Cvi*JI normally cleaves the recognition sequence PuGCPy between the G and C to leave blunt ends. Atypical reaction conditions, which alter the specificity of this enzyme (*Cvi*JI**), yield a quasi-random distribution of DNA fragments form the small molecule pUC19 (2688 base pairs). Fitzgerald *et al.* (1992) quantitatively evaluated the randomness of this fragmentation strategy, using a *Cvi*JI** digest of pUC19 that was size fractionated by a rapid gel filtration method and directly ligated, without end repair, to a lac Z minus M13 cloning vector. Sequence analysis of 76 clones showed that *Cvi*JI** restricts pyGCPy and PuGCPu, in addition to PuGCPy sites, and that new sequence data is accumulated at a rate consistent with random fragmentation.

As reported in the literature, advantages of this approach compared to sonication and agarose gel fractionation include: smaller amounts of DNA are required (0.2-0.5 ug instead of 2-5 ug); and fewer steps are involved (no preligation, end repair, chemical extraction, or agarose gel electrophoresis and elution are needed.

Irrespective of the manner in which the nucleic acid fragments are obtained or prepared, it is important to denature the DNA to give single stranded pieces available for hybridization. This is achieved by incubating the DNA solution for 2-5 minutes at 80-90°C. The solution is then cooled quickly to 2°C to prevent renaturation of the DNA fragments before they are contacted with the chip. Phosphate groups must also be removed from genomic DNA by methods known in the art.

4.22 PREPARATION OF DNA ARRAYS

Arrays may be prepared by spotting DNA samples on a support such as a nylon membrane. Spotting may be performed by using arrays of metal pins (the positions of which correspond to an array of wells in a microtiter plate) to repeated by transfer of about 20 nl of a DNA solution to a nylon membrane. By offset printing, a density of dots higher than the density of the wells is achieved. One to 25 dots may be accommodated in 1 mm^2, depending on the type of label used. By avoiding spotting in some preselected number of rows and columns, separate subsets (subarrays) may be formed. Samples in one subarray may be the same genomic segment of DNA (or the same gene) from different individuals, or may be different, overlapped genomic clones. Each of the

subarrays may represent replica spotting of the same samples. In one example, a selected gene segment may be amplified from 64 patients. For each patient, the amplified gene segment may be in one 96-well plate (all 96 wells containing the same sample). A plate for each of the 64 patients is prepared. By using a 96-pin device, all samples may be spotted on one 8 x 12 cm membrane. Subarrays may contain 64 samples, one from each patient. Where the 96 subarrays are identical, the dot span may be 1 mm^2 and there may be a 1 mm space between subarrays.

Another approach is to use membranes or plates (available from NUNC, Naperville, Illinois) which may be partitioned by physical spacers *e.g.* a plastic grid molded over the membrane, the grid being similar to the sort of membrane applied to the bottom of multiwell plates, or hydrophobic strips. A fixed physical spacer is not preferred for imaging by exposure to flat phosphor-storage screens or x-ray films.

The present invention is illustrated in the following examples. Upon consideration of the present disclosure, one of skill in the art will appreciate that many other embodiments and variations may be made in the scope of the present invention. Accordingly, it is intended that the broader aspects of the present invention not be limited to the disclosure of the following examples. The present invention is not to be limited in scope by the exemplified embodiments which are intended as illustrations of single aspects of the invention, and compositions and methods which are functionally equivalent are within the scope of the invention. Indeed, numerous modifications and variations in the practice of the invention are expected to occur to those skilled in the art upon consideration of the present preferred embodiments. Consequently, the only limitations which should be placed upon the scope of the invention are those which appear in the appended claims.

All references cited within the body of the instant specification are hereby incorporated by reference in their entirety.

5.0 EXAMPLES

5.1 EXAMPLE 1

Novel Nucleic Acid Sequences Obtained From Various Libraries

A plurality of novel nucleic acids were obtained from cDNA libraries prepared from various human tissues and in some cases isolated from a genomic library derived from human chromosome using standard PCR, SBH sequence signature analysis and Sanger sequencing techniques. The inserts of the library were amplified with PCR using primers specific for the vector sequences which flank the inserts. Clones from cDNA libraries were spotted on nylon membrane filters and screened with oligonucleotide probes (*e.g.*, 7-mers) to obtain signature sequences. The clones were clustered into groups of similar or identical sequences. Representative clones were selected for sequencing.

In some cases, the 5' sequence of the amplified inserts was then deduced using a typical Sanger sequencing protocol. PCR products were purified and subjected to fluorescent dye terminator cycle sequencing. Single pass gel sequencing was done using a 377 Applied Biosystems (ABI) sequencer to obtain the novel nucleic acid sequences. In some cases RACE (Rapid Amplification of cDNA Ends) was performed to further extend the sequence in the 5' direction.

5.2 EXAMPLE 2

Novel Contigs

The novel contigs of the invention were assembled from sequences that were obtained from a cDNA library by methods described in Example 1 above, and in some cases sequences obtained from one or more public databases. The sequences for the resulting nucleic acid contigs are designated as SEQ ID NO: 1-30368 and are provided in the attached Sequence Listing. The contigs were assembled using an EST sequence as a seed. Then a recursive algorithm was used to extend the seed EST into an extended assemblage, by pulling additional sequences from different databases (*i.e.*, Hyseq's database containing EST sequences, dbEST version 115, gb pri 115, and UniGene version 103, and exons from public domain genomic sequences predicted by GenScan) that belong to this assemblage. The algorithm terminated when there was no additional sequences from the above databases that would extend the assemblage. Further, the inclusion of component sequences into the assemblage was based on a BLASTN hit to the extending assemblage with BLAST score greater than 300 and percent identity greater than 95%.

The novel predicted polypeptides (including proteins) encoded by the novel polynucleotides (SEQ ID NO: 1-30368) of the present invention are incorporated in the attached Sequence Listing. A subset the predicted polypeptide sequences contain an unknown amino acid, a stop codon, a possible nucleotide deletion or a possible nucleotide insertion. These sequences have been shown in their entirety with the special characters in Table 2. Table 2 also shows the corresponding start and stop nucleotide locations to each of SEQ ID NO: 1-30368. Table 2 also indicates the method by which the polypeptide was predicted. Method A refers to a polypeptide obtained by using a software program called FASTY (available from http://fasta.bioch.virginia.edu) which selects a polypeptide based on a comparison of the translated novel polynucleotide to known polynucleotides (W.R. Pearson, Methods in Enzymology, 183:63-98 (1990), herein incorporated by reference). Method B refers to a polypeptide obtained by using a software program called GenScan for human/vertebrate sequences (available from Stanford University, Office of Technology Licensing) that predicts the polypeptide based on a probabilistic model of gene structure/compositional properties (C. Burge and S. Karlin, J. Mol. Biol., 268:78-94 (1997), incorporated herein by

reference). Method C refers to a polypeptide obtained by using a Hyseq proprietary software program that translates the novel polynucleotide and its complementary strand into six possible amino acid sequences (forward and reverse frames) and chooses the polypeptide with the longest open reading frame.

The nearest neighbor results for SEQ ID NO: 1-30368 were obtained by a BLASTP version 2.0al 19MP-WashU search against Genpept release 121 and Geneseq release 200103 (Derwent), using BLAST algorithm. The nearest neighbor result showed the closest homologue for SEQ ID NO: 1-30368. The nearest neighbor results for SEQ ID NO: 1-30368 are incorporated in the attached Sequence Listing.

Using eMatrix software package (Stanford University, Stanford, CA) (Wu et al., J. Comp. Biol., Vol. 6 pp. 219-235 (1999) herein incorporated by reference), all the sequences were examined to determine whether they had identifiable signature regions. The attached Sequence Listing provodes the results obtained by eMatrix analysis for each polypeptide as follows: the signature region found in the indicated polypeptide sequences, the description of the signature, the eMatrix p-value(s) and the position(s) of the signature within the polypeptide sequence.

Using the pFam software program (Sonnhammer et al., Nucleic Acids Res., Vol. 26(1) pp. 320-322 (1998) herein incorporated by reference) all the polypeptide sequences were examined for domains with homology to certain peptide domains. The attached Sequence Listing provides the results obtained by PFAM analysis for each peptide, namely: the name of the domain found, the description, the p-value and the pFam score for the identified domain within the sequence.

Tables 1 and 2 follow. Table 1 shows the various tissue sources of SEQ ID NO: 1-30368. Table 2 shows the start and stop nucleotides for the translated amino acid sequence for which each assemblage encodes. Table 2 also provides a correlation between the amino acid sequences set forth in the Sequence Listing, the nucleotide sequences set forth in the Sequence Listing and the SEQ ID NO: in USSN 09/540,217

Table 1

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
adult brain	GIBCO	AB3001	39-41 192 197-200 315-316 540-542 576-580 608-622 635 1004 1185-1187 1273-1279 1431 1474 1721-1722 2036 2136-2137 2457 2471-2474 2513 2599-2603 2988-2989 3105-3106 3212 3276-3277 3306-3308 3352 3365 3374-3376 3433 3448-3450 3555-3558 3693 3949-3953 4067-4072 4160-4162 4558-4560 4581-4582 4612-4614 4837-4840 5483-5484 5603-5606 5700 5802 5980-5984 6135-6136 6403-6404 6452-6453 7209-7212 7447-7449 7452-7460 7536-7541 7554-7555 7622-7623 7630-7636 7660-7665 7701-7703 7771 7778-7783 7798-7801 7921-7923 7994 8010-8012 8025-8026 8145-8151 8227-8229 8415 8497-8499 8936-8938 8986-8991 9002-9004 9013-9017 9337-9338 9366-9368 9375-9376 9391-9392 9395-9396 9431-9436 9443 9475-9476 9517-9518 9522-9525 9586-9589 9603-9604 9851-9852 9854-9855 9874-9895 9905-9908 9947-9952 9969-9980 9986-9992 10025-10026 10033-10037 10167-10172 10277 10480-10482 10488-10489 10498-10503 10520-10522 10537-10538 10592-10594 10628-10630 11226-11227 11339-11344 11406-11407 11431-11432 11731-11734 12150-12151 12239 12241-12244 12555-12559 12615-12618 12785-12787 12978-12981 12984-12985 12997-12999 13567-13568 13592-13595 13606-13608 13873-13875 13999-14004 14360-14369 14650-14651 14684-14685 15013-15018 15096 15174-15181 15209-15210 15250-15251 15257 15323-15324 15548-15552 15568-15572 15576-15577 15588-15589 15699-15700 15881-15883 16438-16439 16473-16478 16496-16497 16609-16611 16686-16693 16700-16701 16727-16729 16836-16842 16934-16937 16949-16953 17455-17456 17857-17861 17958-17963 18029-18030 18136-18138 18423-18425 18516-18518 18535-18537 18624-18626 18668-18672 18719-18722 18750-18756 18790-18793 18802-18804 18836-18838 18899-18903 18919-18921 18943-18945 18947-18950 18964-18969 18989-18990 19013-19017 19045-19048 19057-19065 19142-19147 19154-19155 19224 19316-19317 19345-19349 19355-19360 19362 19370 19385-19389 19415-19417 19422-19431 19442-19444 19503 19560-19562 19566 19604-19607 19693 19709-19710 19727-19732 19736-19742 19772 19804-19808 19921-19929 19933-19938 19943-19946 19969-19981 20015-20017 20029-20043 20087-20094 20099-20102 20111-20112 20122-20127 20161-20164 20167-20171 20180-20181 20189-20194 20198-20199 20215-20218 20281-20282 20289 20321-20324 20349-20354 20361 20393-20400 20415-20417 20437-20440 20524-20535 20542-20545 20554-20558 20607-20612 20614-20615 20646-20652 20698-20707 20718-20725 20727-20732 20789-20791 20806-20812 20844-20849 20888-20889 20926 20938-20942 20999-21004 21027-21031 21062-21066 21072-21075 21137-21140 21145-21148 21153-

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
			21154 21272-21274 21277-21283 21410-21414 21434-21439 21485-21491 21495-21500 21647-21655 21729-21733 21929-21935 21958-21961 21973-21974 21978 22000-22006 22026-22029 22040-22041 22087-22088 22101-22107 22141-22143 22160 22250-22252 22284-22289 22309 22314-22317 22336-22342 22347-22348 22358-22359 22372 22405-22408 22495 22534-22539 22634-22643 22653-22654 22661-22662 22665-22667 22671-22674 22700-22701 22794-22796 22805-22809 22887-22891 22899-22900 22948-22950 22952-22953 22982-22986 22991-22994 23059-23060 23071 23141 23249 23251 23329-23337 23412-23414 23489-23490 23492-23493 23508-23509 23543-23544 23704 23834-23835 23890-23892 23959 24014-24018 25289-25290 25319-25321 25374-25375 25966-25968 26205-26206 26258-26259 26303 26316-26321 26327 26337 26373-26374 26596-26601 26788-26789 26843 26850-26852 26897 27067-27070 27100-27102 27150-27151 27247-27251 27304-27305 27439-27440 27493-27495 27636-27639 27750-27754 27814-27818 27861-27864 27890-27892 27989-27990 28099-28100 28311-28313 28424 28426-28428 29278-29283 29409-29416 29444 29718-29721 30141-30142
adult brain	GIBCO	ABD003	30 51-52 144-145 170-171 180-181 202-203 255-256 302 315-316 319-323 326-327 395 406-407 412-413 464-465 540-542 549 553-554 576-578 626-637 652-653 656 697-699 716-717 721-725 785-786 825 847-855 952 967 969-971 1001-1004 1047 1067-1071 1092-1094 1097-1098 1123-1127 1169-1179 1259-1262 1269-1279 1307 1431 1453-1454 1471-1477 1483 1490-1492 1602-1603 1644-1645 1667-1668 1840 1860 1887-1889 1931 1967 1986-1987 2058 2275-2276 2383-2388 2455-2457 2469 2471-2474 2513 2540-2541 2577-2584 2591 2599-2603 2663-2665 2692-2694 2710 2814-2815 2926 2937-2938 2975-2977 3001 3006-3008 3090 3151-3154 3205-3207 3366 3433 3451 3472-3473 3531-3534 3555-3558 3590 3624 3635 3671-3672 3685 3705-3706 3735-3736 3949-3953 4053-4054 4080-4082 4124-4126 4406-4407 4489-4493 4517-4522 4562-4573 4623-4639 4785-4789 4845-4851 4857-4861 4874-4889 4897-4898 4971-4974 5092-5094 5267-5268 5291-5294 5335-5336 5480-5482 5608-5609 5700 5762 5802 5808-5812 5919-5921 5956-5957 5980-5984 5986-5988 6011-6021 6140-6143 6293-6296 6400 6403-6404 6406-6410 6651-6653 6662-6664 6791-6794 6877-6878 6932-6938 7214-7215 7245-7248 7447-7449 7536-7541 7611-7612 7624-7629 7640-7642 7668-7670 7695-7696 7757-7759 7771 7778-7786 7789-7793 7798-7801 7890 7898-7900 7976 7986-7987 7995-7998 8002 8017-8019 8049-8056 8069 8117-8121 8152-8156 8162 8174-8177 8182-8183 8242-8246 8250 8301-8306 8343-8344 8351-8360 8363-8366 8368-8370 8409-8414 8497-8499 8512-8513 8543-8550 8607-8609 8612-8616 8754-8759 8762-8766 8768-8770 8777-8779 8917-8918 9013-9017 9031-9035 9038-9045 9063-9067 9072-9074 9306-9313 9321-9323 9375-9376 9391-9392 9406-9407 9437-

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
			9440 9444-9445 9454-9455 9517-9518 9531 9561-9562 9603-9604 9729-9731 9733-9738 9757-9758 9763-9767 9826 9828-9832 9851-9852 9854-9855 9864-9866 9874-9897 9923-9924 9947-9953 9956-9957 9969-9980 10011 10015-10016 10033-10040 10167-10172 10265-10272 10277 10306 10449-10450 10470-10473 10498-10503 10537-10542 10592-10594 10607-10608 10612-10614 10624-10626 10628-10630 10638-10639 10870-10875 10881-10883 10886-10889 10891-10893 10895-10898 10904-10905 10913-10914 10980-10985 11035-11037 11066-11068 11081 11123-11124 11274-11275 11295-11299 11339-11350 11419-11422 11465-11466 11582-11583 11586-11602 11607-11608 11679 11693-11695 11731-11734 11749-11750 11775-11776 11780-11782 11803-11804 11835-11836 11840 11842-11855 11901-11905 11937-11938 12042-12044 12121-12126 12131-12132 12150-12151 12186-12189 12194-12196 12206-12208 12283-12284 12361 12555-12559 12573-12574 12581-12582 12615-12618 12637 12653-12654 12673-12675 12723 12760-12762 12785-12787 12796-12798 12805-12806 13077-13079 13083-13086 13576-13579 13592-13595 13603-13612 13638-13641 13664 13865-13866 13885-13887 13903-13905 13994-13997 14008-14020 14023-14026 14044-14045 14130-14131 14141-14142 14187-14195 14264-14265 14268-14269 14299-14301 14313-14317 14346 14360-14369 14604 14607-14609 14640-14642 14650-14651 14684-14685 14789-14791 15019-15024 15093-15095 15182-15183 15218-15219 15257-15259 15290-15291 15406-15407 15486-15489 15532-15535 15543-15546 15553-15556 15576-15577 15588-15589 15631-15632 15699-15700 15988-15990 16006-16015 16044-16046 16075-16079 16086-16088 16107-16109 16172 16397-16398 16422-16429 16451-16452 16470-16478 16498-16500 16609-16611 16636-16637 16642 16652 16698-16705 16836-16842 16934-16939 17010-17014 17284-17285 17330-17332 17963 18015-18016 18029-18030 18136-18138 18400-18402 18419-18420 18423-18425 18492-18494 18516-18518 18527 18533-18537 18617 18625-18626 18633-18637 18671-18672 18689-18692 18717-18722 18750-18756 18759-18761 18771-18772 18778-18793 18796 18802-18804 18811-18813 18822-18824 18856-18880 18882-18888 18899-18903 18919-18921 18934-18939 18941 18947-18951 18955-18959 18975-18977 18989-18990 18993-18996 19005-19009 19013-19018 19045-19048 19057-19058 19062-19065 19074-19080 19102-19105 19142-19147 19154-19155 19159 19209-19210 19213-19220 19251-19252 19257 19260-19262 19266-19267 19306-19309 19316-19317 19355-19360 19362-19364 19370 19373-19374 19380-19384 19387-19389 19395-19400 19415-19417 19422-19434 19442-19444 19446-19448 19461 19487 19526-19529 19536 19560-19562 19566 19604-19607 19626 19656-19657 19667-19668 19693 19698 19709-19710 19727-19742 19759-19763 19800-19808 19813-19815 19921-19929 19933-

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
			19946 19953-19957 19962-19963 19972-19981 20029-20043 20072-20079 20099-20102 20106-20112 20114-20120 20130 20146-20148 20151-20154 20161-20164 20167-20171 20180-20194 20198-20207 20222-20225 20235-20240 20257-20262 20265-20278 20289 20316 20321-20324 20328-20330 20345-20354 20360 20393-20400 20415-20420 20425-20431 20441-20446 20469-20474 20476-20479 20485-20490 20502-20503 20505-20510 20514-20520 20542-20545 20548-20557 20559-20562 20568 20607-20612 20614-20619 20644-20645 20649-20671 20681 20683-20685 20689-20692 20698-20707 20712-20713 20718-20725 20753 20758-20767 20789-20797 20806-20812 20824-20849 20863 20897-20900 20927-20928 20938-20942 20952-20954 20999-21004 21027-21045 21062-21066 21069-21075 21105-21111 21141-21142 21153-21154 21171-21174 21197-21198 21202-21207 21225-21226 21229-21235 21237-21247 21256-21262 21272-21274 21277-21280 21297-21298 21301-21303 21351-21352 21434-21439 21446-21450 21467-21469 21485-21491 21647-21655 21712-21717 21729-21733 21881-21885 21899-21902 21905-21910 21917-21921 21924 21929-21938 21948-21950 21955-21957 21971-21972 21978-21982 22000-22015 22020-22029 22042-22046 22080-22088 22090-22094 22101-22107 22117-22119 22141-22151 22160 22169-22170 22187-22192 22208-22226 22230 22251-22252 22261-22264 22277-22289 22300-22302 22318 22329-22332 22343-22350 22358-22359 22365-22371 22373 22381-22388 22399-22404 22409-22410 22434-22435 22440-22448 22495 22559 22571-22581 22607-22609 22644-22651 22653-22654 22661-22662 22665-22667 22671-22674 22703-22706 22760-22762 22794-22796 22823-22829 22857-22858 22870-22874 22881-22893 22923-22924 22948-22954 22973 22982-22986 23007-23021 23047-23052 23070 23080-23083 23112-23116 23212-23215 23229-23233 23237-23239 23249 23251 23329-23337 23343-23344 23382-23390 23399 23412-23421 23486-23487 23489-23490 23492-23493 23495-23496 23508-23509 23704 23718-23721 23726-23730 23761-23763 23771-23780 23800 23802-23809 23816-23819 23827-23833 23836-23837 23843-23844 23878-23880 23890-23892 23941-23956 23959 24005-24011 24014-24018 24021-24024 24772-24774 25085-25090 25279-25290 25307-25308 25319-25322 25373-25375 25403-25407 25598-25603 26196-26199 26209-26213 26217-26218 26221-26223 26237-26239 26258-26259 26266 26304 26327 26337 26347-26348 26350-26352 26359-26365 26373-26374 26376-26377 26395 26423 26469-26470 26596-26601 26665-26666 26681-26683 26691-26694 26736 26755-26756 26788-26789 26844-26845 26876-26879 27044-27047 27053-27057 27067-27070 27100-27102 27105 27133-27134 27193-27200 27206 27209-27213 27218 27254-27260 27269-27270 27281-27282 27299-27301 27304-27305 27334 27340-27342 27493-27495 27501-27503 27544-27545 27574-

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
			27577 27600-27606 27700-27701 27814-27815 27823-27824 27861-27864 27890-27892 27940-27942 27970 28040-28041 28099-28100 28142-28145 28186 28263-28268 28286 28311-28313 28324-28345 28361-28362 28424 29301-29303 29328-29337 29339-29340 29343-29345 29409-29416 29594-29604 29718-29721 29940-29949 29960-29961 30141-30142 30150-30156 30218-30220 30233-30235 30240-30242
adult brain	Clontech	ABR001	15 227-230 329-330 414-418 716-717 934-935 1136-1139 1436-1437 1472-1473 1505-1506 1593-1594 2058 2132-2137 2139-2142 2378-2381 2407 2550-2552 2577-2584 2587-2588 3094-3096 3221-3222 3377 3414-3417 3526-3529 3861 3949-3953 4340-4341 4515-4516 4574-4576 4857-4861 4986-4987 5092-5094 5654 5700 5864-5866 5992 6140-6143 6540-6541 6570-6571 6814-6831 7668-7670 7802-7804 7994 8008-8009 8017-8019 8111 8129-8131 8160 8162 8242-8246 8368-8369 8453-8454 8512-8513 8762-8766 8982-8983 9339 9391-9392 9510-9516 9531 9666 9682-9683 9828 10167-10172 10312 10520-10522 10913-10914 10959-10962 11064 11071-11075 11345-11350 11805-11808 11835-11836 11900 11937-11938 12050-12056 12194-12197 12796-12798 13925-13926 14604 14714-14717 14785-14786 15182-15183 15400-15403 15462-15463 15545-15546 15563-15564 16123-16128 16174-16176 16570-16573 16601 16623 16642 16851-16853 16924 16934-16937 17963 18015-18016 18046-18048 18500-18501 18516-18518 18535 18655-18658 18671-18672 18762-18766 18955-18959 19018 19045-19048 19207-19208 19257 19350 19380-19384 19447-19449 19484-19486 19526-19529 19659-19661 19670-19671 19706-19710 19764-19767 19804-19808 19924-19925 19962-19963 19965-19967 20120 20189-20194 20231-20234 20271-20273 20412-20413 20441-20446 20456-20468 20485-20494 20521-20523 20676-20680 20710-20711 20718-20725 20733-20734 20747-20751 20824-20826 20836-20843 20926 21060-21061 21069-21075 21105-21111 21153-21154 21353-21354 21410-21414 21454-21457 21554-21556 21647-21655 21924 21929-21935 22003-22015 22040-22041 22045-22046 22077-22083 22108-22116 22165-22168 22246-22249 22284-22289 22373-22374 22411-22432 22625-22628 22637-22643 22671-22674 23080-23083 23112-23119 23141 23201-23202 23358-23360 23412-23418 23526-23531 23761 23793-23797 23802-23805 23878-23880 24014-24018 24105-24113 24116 25403-25407 26232-26233 26270-26272 26285-26290 26685-26686 27012-27014 27028-27029 27098-27099 27377-27378 27493-27495 27544-27545 27623 27640-27641 27729-27739 27840-27844 27970 28361-28362 28424 29427-29438 30233-30235
adult brain	Clontech	ABR006	21 360-361 510-511 546-547 579-580 792-795 969-971 1165-1168 1228-1231 1252-1256 1453-1454 1472-1473 1681-1687 1975-1977 2044-2045 2214-2219 2231-2232 2270-2271 2306 2396-2400 2458 2826-2827 2951-2955 3158 3274-3275 3313-3314 3326-3331 3483-3484 3686

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
			3856-3857 3939-3941 4080-4082 4091-4095 4173 4441-4443 4484-4485 4765-4773 4785-4789 4795-4809 4988 4992 5364 5930-5931 5971-5972 6155-6159 6450-6451 7353-7367 7374 7580-7597 7701-7703 7784-7786 7972-7975 8020 8101-8104 8106 8152-8156 8162 8184-8185 8342 8370 8489 8758-8759 8936-8938 8978-8981 9009-9017 9029-9030 9063-9067 9069-9078 9306-9311 9339 9479-9485 9517-9518 9828 9874-9895 9909-9912 10033-10037 10254-10261 10498-10503 10523-10532 10624-10639 10923-10926 10936-10937 11328-11331 11708-11710 12573-12574 12743-12750 12785-12787 13556-13559 13660-13675 13847-13849 14054-14056 14170-14172 14347-14348 14390 14604 14666-14668 14996 15097 15257 15283-15286 15336-15340 15397-15398 15576-15577 15886-15887 15896-15905 16022-16023 16237 16461-16464 16496-16497 16623 16643-16648 16652 16752-16753 17238-17241 17369-17370 17937-17939 17956-17957 18029-18030 18044-18045 18049-18064 18393-18394 18411-18418 18423-18425 18527 18536-18537 18719-18722 18762-18766 18778-18780 18829-18834 18899-18903 18934-18935 19001-19004 19159 19207-19208 19211-19212 19221-19222 19273 19350 19484-19486 19670-19671 19698 19727-19732 19736-19742 19800-19808 19814-19815 19855-19856 19939 19943-19946 19951-19952 19972-19980 20069-20071 20087-20094 20099-20102 20122-20127 20157-20181 20200-20207 20274-20278 20316 20321-20324 20414 20441-20446 20456-20468 20491-20494 20524-20535 20542-20545 20547 20554-20557 20607-20612 20676-20680 20718-20725 20747-20751 20897-20900 21005-21008 21069-21071 21088-21096 21145-21148 21157-21169 21171-21174 21176-21180 21213-21215 21241-21247 21263-21266 21272-21274 21277-21280 21343-21350 21377-21397 21463-21465 21554-21556 21911-21912 21929-21935 21955-21957 21973-21974 21978 22007-22015 22019 22045-22046 22070-22076 22080-22088 22090-22091 22108-22114 22120-22127 22135-22138 22144-22151 22158-22159 22246-22249 22284-22289 22347-22348 22375-22382 22389-22432 22625-22628 22653-22654 22671-22674 22833-22834 22881-22886 22916-22922 23007-23021 23071 23080-23083 23223-23225 23229-23233 23358-23360 23379-23381 23412-23414 23434-23438 23486 23506-23507 23543-23544 23555-23565 23771-23780 23827-23833 23841-23844 23941-23956 24035-24040 25213-25219 25279-25290 25315 25383-25415 26235-26236 26280 26310-26314 26337 26361-26365 26409-26410 26425-26427 26603 26687 26860-26862 27067-27070 27100-27102 27105 27193-27200 27209-27213 27441-27443 27562-27563 27589-27592 27821-27822 27825-27838 28146-28147 28296 28464 29328-29331 29343-29345 29409-29416 29439-29445 29940-29949 30205 30221-30223
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Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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adult lung	GIBCO	ALG001	112 156 197-200 227-230 273-278 310-314 332 373-374 419-420 459-460 505 524-525 532-533 549 576-578 635 669 692-693 716-717 845-848 891 919-922 945-946 1028 1064-1066 1071 1136-1139 1158-1161 1235-1237 1307 1411-1413 1431-1435 1705-1714 1721-1722 1792-1794 1879-1880 1986-1987 2072 2202-2203 2299 2306 2599-2603 2886-2887 2975-2977 3195-3197 3273-3275 3281-3282 3433 3487-3503 3550-3554 3686 3731-3732 3820-3821 3840-3852 4489-4493 4612-4614 4720-4725 5057-5059 5335-5336 5557-5560 5801-5804 5846 5919-5921 6170 6400 6405 6791-6794 7056-7057 7209-7212 7536-7541 7654-7655 7660-7665 7693-7694 7742-7743 7747-7751 7806-7808 7812-7818 7988 8079 8263-8265 8339-8341 8349-8360 8368-8369 8430-8433 8466-8476 8497-8499 8510-8511 8688 8917-8918 9072-9074 9306-9311 9340-9342 9408-9414 9456-9458 9531 9615-9616 9815-9820 9835-9840 9851-9852 9874-9895 9899-9901 9989-9992 10017-10019 10038-10040 10277 10306 10498-10503 10520-10522 10550 10592-10594 10603-10606 10759-10764 10873-10875 10895-10898 10980-10985 11123-11124 11212-11216 11339-11344 11359-11369 11372-11396 11399-11402 11423-11426 11431-11432 11473-11474 11476-11478 11495 11578 11609 11658-11659 11669-11671 11711-11712 11731-11734 11809 12140 12150-12151 12186-12189 12241-12244 12258 12374-12377 12470-12471 12519-12540 12555-12559

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lymph node	Clontech	ALN001	167 170-171 180-181 302 332 395 425-427 505 635 670-671 849-851 919-922 973-987 998-1000 1028 1047 1086-1087 1232-1234 1259-1262 1273-1279 1307 1456-1460 1499 1569-1570 1667-1668 1705-1714 1879-1880 1943 2063-2065 2126-2129 2272-2274 2404-2406 2409 2471-2474 2533 3151-3154 3322-3323 3377 3461-3463 3512-3514 3737 3822 3834-3835 3879-3880 4255 4555-4556 4562-4568 5335-5336 5572-5573 5580 5650-5651 5802 5805-5807 5910-5911 6403-6404 6832-6850 7216-7219 7447-7449 7643-7647 7654-7655 7697 7744-7746 7757-7759 7763-7770 7890 7972-7975 7978-7985 8010-8012 8342 8698-8700 9043-9045 9306-9311 9475-9476 9487-9488 9531 9615-9616 9780-9781 9916-9920 10273-10274 10306 11123-11124 11295-11296 11339-11344 11431-11432 11476-11478 11538-11540 11607-11608 11696 11780-11782 11835-11836 12140 12150-12151 12374-12377 12545-12546 12615-12618 12642-12644 12723 12760-12762 12782-12784 12796-12798 12872-12881 13077-13082 13592-13595 13906 14304-14305 14546-14549 15182-15183 15190-15191 15290-15291 15545-15546 15548-15550 15576-15577 15699-15700 16044-16046 16110-16112 16284-16289 16370-16374 16536-16538 16545 16609-16611 16628-16631 16636-16637 16642 16652 16954-16961 17046-17057 17131-17132 17330-17332 17454-17456 17958-17962 18015-18016 18029-18030 18405-18406 18411 18533-18534 18579-18581 18617 18719-18726 18750-18758 18771-18772 18778-18780 18789 18805 18811-18813 18822-18824 18836-18838 18846-18853 18899-18903 18975 18996 19018 19062-19065 19090 19122-19131 19138-19140 19154-19155 19211-19212 19274 19283-19294 19370 19380-19384 19390-19394 19401-19402 19415-19417 19442-19444 19503 19526-19529 19688 19693 19706-19708 19743-19751 19813-19815 19915-19918 19921-19923 19948-19949 19972-19980 20048-20052 20066-20068 20106-20110 20161-20164 20172-20179 20182-20188 20235-20240 20257-20262 20437-20440 20558 20563-20567 20767 20924-20925 20938-20942 21027-21031 21233-21235 21277-21280 21377-21402 21480-21482 21495-21500 21529-21530 21587-21646 21978-21982 22115-22116 22141-22143 22160 22277-22283 22312-22313 22336-22342 22358-22359 22373 22455-22465 22644-22651 22668 22690 22700-22701 22732-22735 22737-22739 22823-22827 22838-22842 23046 23070 23074-23076 23098-23101 23237-23239 23379-23381 23433 23448-23450 23473-23474 23486 23492-23493 23495-23496 23508-23509 23526-23531 23761 23802-23805 23999-24001 24014-24018 24772-

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young liver	GIBCO	ALV001	10-14 165-166 170-171 202-203 218-219 324-325 332 461-463 534-535 582-584 674-676 847-848 900-904 1035-1037 1058-1060 1123-1127 1346-1347 1431 1470 1478 1527-1528 1705-1714 1778-1779 1908-1909 1967 1980-1982 2015-2018 2284-2298 2570-2574 2599-2603 3255-3259 3276-3277 3374-3376 3507 3512-3514 3518-3520 4091-4095 4160-4162 4273-4274 4343-4346 4370-4371 4515-4516 4562-4568 4600-4601 4640-4643 4857-4861 5152-5153 5335-5336 5370 5512-5516 5519-5521 5572-5573 5899-5902 5997-6000 6011-6021 6400 6572-6574 6585-6592 6791-6794 7209-7212 7214-7215 7258-7263 7426-7442 7536-7541 7630-7636 7648-7653 7671-7673 7681-7687 7701-7703 7742-7743 7778-7783 7798-7805 7815-7818 7930-7932 7947-7948 7995-7997 8017-8019 8079 8113-8114 8145-8151 8157-8159 8187-8200 8242-8246 8250 8342 8349-8350 8377-8379 8434-8452 8461-8464 8497-8499 8502-8503 8512-8513 8543-8550 8554-8555 8607-8609 8689-8690 8758-8759 8762-8766 9317-9318 9391-9392 9395-9396 9460 9475-9476 9478 9522-9525 9531 9558 9561-9562 9585-9589 9617-9626 9719-9722 9829-9832 9848-9850 9854-9855 9874-9895 9902-9904 9929-9935 9965-9968 9984-9985 10167-10172 10265-10267 10277 10484-10487 10520-10522 10588-10591 10907-10912 10936-10937 10966 11314-11315 11406-11407 11431-11432 11468-11472 11495 11741-11742 11803-11804 11840 11890-11891 12140 12173 12177-12181 12637 12723 12829-12830 12948-12962 13077-13079 13638-13641 13865-13866 13873-13875 13999-14003 14054-14056 14692-14693 14784 14789-14791 15011-15012 15019-15024 15096 15182-15183 15218-15219 15243-15248 15250-15251 15290-15291 15381-15385 15406-15407 15412-15414 15530-15531 15548-15550 15576-15577 15588-15589 15591-15592 15863-15866 16168-16171 16177-16181 16365-16366 16484-16486 16545 16550-16552 16601 16636-16637 16642-16648 16652 16702-16703 16710-16712 16752-16753 16851-16853 16878-16881 16894-16896 16913-16915 16934-16937 17026-17028 17284-17285 17330-17332 17857-17861 17955 18001-18003 18029-18030 18069-18072 18207-18210 18421-18422 18500-18501 18527 18536-18537 18642-18643 18668-18677 18719-18722 18730-18732 18745-18758 18761 18773-18777 18789 18796 18829-18834 18857-18880 18906-18907 18925-18933 18942 18955-18959 18976-18977 19029-19035 19221-19222 19224-19225 19228-19229

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Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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Genomic clones from the short arm of chromosome 8	Genomic DNA from Genetic Research	EPM003	1604-1607 4008-4036 4049-4051 4180-4190 4923-4928 5242 5326-5330 7067-7087 7093 7175-7177 7426-7442 7475 8807-8813 8822-8835 8839-8846 8850-8853 8855-8858 8862 8870-8873 8876 8892-8898 9088-9099 9152-9181 9205-9208 9226-9229 9239-9257 9259 9294-9296 9301-9304 10343 10347-10350 10443-10444 10726-10727 10759-10764 10775-10777 10842-10867 13000-13004 13307-13308 13341 13422-13423 13425-13495 13730-13735 13737-13750 13823 14981-14983 15110-15111 15120-15123 15718-15725 15815-15817 15827-15833 15939-15943 15966-15968 15991-15996 16016-16018 17606-17608 17701 17836 17857-17874 17876-17887 17891-17894 18097-18134 18145-18151 18155-18156 18184 18255-18263 18291-18292 18335-18340 18354 21549-21553 21573-21586 21660-21711 21728 21788-21799 21863-21876 22525-22530 22596-22598 22605-22606 22658-22660 24187-24193 24227 24358-24369 24436-24438 24473-24480 24607-24609 24722-24726 24749-24771 24795-24816 24869-24870 24908-24923 24963 25017-25048 25052-25060 25078-25084 25091-25100 25114-25139 25147-25170 25187-25192 25247-25248 25359-25363 25461-25470 25489-25494 25515-25521 25539-25550 25572-25593 25623 25633-25650 25676-25679 25728-25732 25741-25782 25883-25889 25901-25902 25906-25911 25957-25959 25969-26016 26059-26067 26136-26138 26150-26152 26157-26164 26629-26653 27943-27947 28522-28524 28533-28539 28571 28607-28614 28646-28650 28709-28719 28748 28754-28760 28768-28781 28809-28814 28822-28824 28882-28887 28914-28916 28933-28935 29012 29031-29038 29071-29082 29087-29095 29104-29107 29116-29141 29154-29158 29327 29446-29450 29492-29494 29590-29605 29614-29620 29630 29645-29654 29663-29678 29686-29703 29741-29742 29763-29836 29842-29869 29879 29902-29911 29964-29968 30002-30003 30048-30052 30084-30093 30118-30134 30145-30149 30167-30177 30179-30182 30201-30204 30236-30239 30254-30255 30275-30281 30343-30347
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fetal brain	Clontech	FBR001	202-203 847-848 1097-1098 1259-1262 1721-1722 2404-2406 2951-2955 5276-5278 5802 7902-7903 8377-8379 9196-9200 9443 9828 9969-9980 10273-10274 10326-10328 10876 10976-10978 11024-11025 11476-11478 11731-11734 11803-11804 12127-12128 12150-12151 13107-13117 13581-13583 14604 17366-17368 17455-17456 18627-18628 18964-18969 19018 19211-19212 19362 19387-19389 19401-19402 20328-20330 20345-20348 20554-20557 21256-21266 21377-21397 21434-21439 21978 22141-22143 22200-22203 22637-22643 22899-22900 23222 23709 23893-23902 25416-25417 26307-26309 26329 26831 27113 27245-27246 27386-27389 27976-27982 28186 30141-30142
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fetal brain	Clontech	FBR006	3-4 168 192 197-200 240-250 324-325 329-330 362 373-374 464-465 532-535 553-554 576-578 613-614 713-715 847-848 912 927 934-935 949-950 1044-1045 1071 1097-1098 1203-1204 1235-1237 1273-1279 1304 1411-1413 1488-1489 1569-1570 1591-1592 1678-1687 1705-1714 1923-1924 1977 2023-2029 2145 2228 2231-2253 2259-2264 2356 2375 2396-2400 2404-2406 2431 2437-2439 2475 2525-2528 2599-2603 2656-2658 2663-2665 2707-2716 2720-2732 2734-2745 2770-2772 2808-2811 2871-2873 2889-2891 2931-2935 2951-2955 3001 3039 3080-3081 3105-3106 3205-3207 3213 3261-3263 3377 3477-3478 3507 3512-3514 3555-3558 3596 3671-3673 3683 3687-3691 3693 3708 3711-3712 3729-3730 3781-3784 3809 3939-3941 3949-3953 4055-4061 4065 4091-4100 4122-4126 4137-4139 4209-4210 4542 4562-4568 4574-4576 4667 4673 4683-4684 4720-4725 4765-4773 4795-4809 4845-4851 4854-4856 4870-4871 4948 4964-4965 4970 5136-5137 5139 5246 5251-5252 5291-5294 5392 5532-5533 5557-5560 5567-5568 5594-5602 5744-5747 6011-6021 6137 6155-6161 6209-6211 6217-6222 6378-6388 6393-6395 6406-6410 6452-6453 6488-6490 6513-6515 6542-6543 6669-6670 6674-6675 6775-6778 7194-7197 7220-7227 7236-7237 7264-7266 7350-7352 7364-7365 7426-7442 7452-7460 7482-7517 7557-7559 7580-7597 7604-7605 7630-7636 7657-7659 7695-7696 7745-7746 7778-7783 7787-7788 7898-7900 7946 7957 7986-7987 7993 8013-8016 8079 8137-8141 8152-8156 8162-8173 8187-8200 8204-8205 8211-8213 8230-8233 8247-8249 8263-8265 8301-8310 8313-8314 8320-8322 8335-8336 8347-8348 8351-8360 8371-8374 8383-8389 8420-8421 8426-8428 8457-8458 8461-8465 8497-8499 8506 8512-8513 8588-8597 8607-8609 8688 8733-8735 8758-8759 8762-8766 8919-8933 8936-8945 8974-8977 8982-8983 8998-9004 9029-9030 9043-9045 9068 9306-9311 9380-9381 9510-9518 9529-9531 9585 9603-9604 9729-9731 9763-9767 9799-9800 9808-9812 9829-9832 9929-9935 9958-9959 9969-9980 9989-9992 9997-10009 10015-10016 10033-10037 10449-10453 10477-10478 10483 10513-10518 10523-10530 10537-10538 10603-10608 10638-10639 10780-10782 10901-10902 10931-10933 10965 11026 11081 11123-11124 11317 11345-11350 11465-11472 11476-11478 11577 11672 11711-11712 11731-11734 11739-11740 11803-11804 11934 12102-12110 12117-12118 12131-12132 12202-12208 12215-12217 12226-12228 12333-12334 12374-12377

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Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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induced neuron cells	Stratagene	NTD001	188-191 289-291 576-578 617-618 716-717 1030 1034 1097-1098 1646 2540-2541 2599-2603 2675-2678 2724-2726 2871-2873 2973 3326-3331 3374-3376 3649-3653 3908-3910 3930 3949-3953 4165-4170 4486-4487 4515-4516 4581-4582 4984-4985 5053-5054 5272-5275 5335-5336 5777-5778 5802 5919-5921 5980-5984 6403-6404 6787-6790 6795-6800 7170-7172 7258-7263 7325-7343 7363 7368-7369 7557-7559 7688-7689 7693-7694 7701-7703 7745-7746 7778-7783 7906-7912 7990-7992 8187-8200 8250 8497-8499 8689-8690 8758-8759 8998-9001 9029-9030 9040-9042 9047-9048 9087 9321-9323 9559-9560 9829-9832 9909-9912 9947-9952 9993-9996 10477-10478 10494 10531-10532 10592-10594 10615-10623 10842-10867 10980-10985 11045 11228-11229 11314-11315 11405 11431-11432 11541-11543 11546 11609 11700-11707 11739-11740 11803-11808 11886-11891 11941-11944 12131-12132 12241-12244 12258-12262 12898-12899 12902-12905 12997-12999 13592-13595 13609-13612 13652-13659 14304-14305 15182-15183 15190-15191 15290-15291 15588-15589 15969-15974 16028-16029 16180-16181 16545 16619-16621 16642 17292-17296 17401-17432 17435 17455-17456 18029-18030 18097-18134 18300-18307 18400-18402 18412-18418 18691-18692 18771-18772 18796-18801 18839-18841 18846-18853 18899-18903 18989-18990 19001-19004 19012 19074-19080 19106-19118 19207-19208 19256-19257 19266-19267 19306-19307 19316-19317 19343 19355-19360 19387-19389 19447-19448 19458-19460 19488-19493 19566 19598-19601 19617-19619 19659-19661 19736-19742 19804-19808 19813 19939 19972-19980 20029-20043 20099-20102 20106-20110 20114-20119 20122-20127 20182-20188 20208-20218 20485-20490 20521-20523 20607-20612 20681 20698-20707 20827-20835 20853-20854 20871 21105-21111 21248-21271 21275-21280 21284-21294 21463-21465 21495-21500 21587-21646 21929-21935 22020-22025 22045-22046 22070-22073 22141-22143 22160 22187-22192 22195-22198 22243-22245 22358-22359 22365-22371 22381-22388 22433 22653-22654 22671-22674 22690 22916-22922 22977 23201-23202 23251 23358-23360 23420-23421 23700-23701 23798-23799 23806-23809 23890-23892 24749-24754 24928-24938 24985-24988 25029-25040 25279-25288 25376-25379 26024-26028 26205-26206 26209-26213 26266 26280 26310-26314 26327 26361-26365 26678-26680 27091 27100-27102 27269-27270 27446-27449 27522-27539 27544-27545 27729-27739 27861-27864 27896-27927 27989-27990 28315-28316 28361-28364 29117-29123 29328-29337 29343-29345 29418-29419 29426-29431 29885-29891 30167-30177 30352 30361-30368

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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neuronal cells	Stratagene	NTU001	240-250 373-374 425-427 576-578 847-848 1388-1401 1432-1435 1470 1499 1778-1779 2306 2599-2603 2944 3040-3076 3107-3108 3326-3331 3421-3422 3477-3478 3483-3484 3789-3794 3912-3915 4055-4058 4171-4172 4206-4208 4515-4516 4562-4568 4581-4582 4785-4789 5186-5189 5253-5266 5272-5275 5279-5283 5525-5526 5943-5945 6135-6136 6403-6404 7264-7266 7346-7352 7784-7786 7815-7818 8203 8227-8229 8465 8497-8499 8716-8718 8998-9004 9007-9008 9038-9039 9049-9068 9472-9474 9479-9481 9535-9537 9594-9602 9735-9738 9929-9935 9969-9980 10161-10163 10167-10196 10516-10518 10615-10623 10873-10875 10915-10918 11308-11310 11334-11335 11775-11776 11840 12150-12151 12258 12590-12592 12653-12654 12716-12719 12997-12999 13552-13555 13638-13641 13847-13849 14038-14041 14044-14045 14137-14138 14277-14280 14640-14642 14814-14815 15025-15069 15100-15109 15277-15278 15408-15411 15530-15531 15563-15564 15576-15577 15588-15589 15863-15870 16141-16143 16174-16176 16182-16189 16545 16642 16652 16836-16842 16851-16853 17284-17285 17435-17440 17451-17454 17958-17962 18029-18030 18043 18097-18134 18500-18501 18562-18576 18671-18672 18796-18801 18825-18828 18857-18880 18925-18933 18975 18993-18995 19049-19053 19153 19298-19300 19306-19307 19316-19317 19351-19354 19370 19375-19379 19395-19400 19415-19417 19432-19434 19511 19515-19521 19526-19529 19564-19566 19625 19659-19661 19683-19687 19813-19815 19855-19856 19938 19940-19942 19965-19967 19972-19980 20026-20027 20099-20102 20106-20110 20161-20164 20200-20207 20241 20289 20336-20338 20406-20407 20437-20440 20485-20490 20521-20523 20537-20541 20602-20612 20631-20634 20639-20640 20646-20648 20666-20671 20792-20797 20827-20843 20871 20897-20900 20924-20925 20927-20928 20938-20942 20957-20962 21032-21045 21208-21210 21241-21247 21256-21262 21272-21283 21295-21296 21554-21556 21587-21655 21899-21904 21936-21938 21951-21954 21958-21966 22007-22015 22040-22041 22047-22049 22070-22073 22152-22156 22165-22168 22171-22175 22218-22224 22243-22245 22253-22255 22292-22299 22312-22313 22343-22346 22372-22373

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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pituitary gland	Clontech	PIT004	307-308 395 845-846 1440-1447 1451 1453-1454 2272-2274 2362-2363 3105-3106 3322-3323 3433 4080-4082 4612-4614 4714-4719 4971-4974 5284 5335-5336 5572-5573 6140-6143 6405 6488-6489 7216-7219 7611-7612 7988 8343-8344 8917-8918 9007-9008 9029-9030 9444 9759-9762 10451-10453 10640-10644 10873-10875 11649-11650 11660-11661 11731-11734 11803-11804 11835-11836 12361 12637 13077-13079 13592-13595 14261-14263 14723-14724 15093-15095 15190-15191 15392-15396 16141-16143 16422-16429 16636-16637 16642 16894-16896 18691-18692 18836-18838 18899-18903 18975 19074-19080 19260-19262 19362 19415-19417 19458-19460 19921-19923 20161-20164 20452-20455 20548-20553 20575-20578 20629-20630 20666-20671 21072-21075 21149-21151 21256-21262 21881-21885 21955-21957 22160 22187-22192 22199 22358-22359 22375-22376 22383-22388 22644-22651 22768-22770 22805-22809 22852-22853 22991-22994 23080-23083 23242-23244 23704 23720-23721 23761 26196-26199 26327 26361-26365 26431 26755-26756 27067-27070 27254-27260 27755-27756 27825-27826 27861-27864 28311-28313 29332-29337 29360-29362 29370 30085-30087 30141-30142 30150-30156
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Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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rectum	Invitrogen	REC001	180-181 534-535 540-542 1681-1687 1705-1714 1721-1722 1745-1746 2272-2274 2675-2678 2695-2698 2813-2846 3326-3331 3555-3558 3687-3691 3717-3720 3834-3835 3949-3953 4692-4695 4857-4861 5246 5337-5341 5572-5573 5802-5804 5919-5921 6209-6211 6400-6404 6406-6410 7209-7212 7426-7442 7609 7747-7751 7757-7759 7778-7783 8074-8078 8323-8325 8329-8334 8453-8454 8741-8750 8986-8991 9029-9030 9043-9045 9305 9375-9376 9391-9392 9456-9458 9531 9585 9828 9921-9922 9986-9988 10263-10264 10277 10306 10480-10482

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salivary gland	Clontech	SAL001	260 307-308 331 551-552 832-836 969-971 981-985 1312-1313 1721-1722 1810-1811 2072 2303 2306-2307 2599-2603 2847 2850-2860 3151-3154 3657 3723-3728 3737 3840-3852 3949-3953 4515-4516 4531-4533 4555-4556 4581-4582 4857-4861 4971-4974 5269-5271 5525-5526 5652-5653 5658 5700 6337-6338 6411-6412 6442-6449 6762-6764 7452-7460 7678-7687 7701-7703 7745-7746 7778-7783 7805 7988 8145-8151 8187-8200 8337-8342 8383-8389 8554-8555 8986-8991 9018-9020 9038-9039 9427-9428 9531 9535-9537 9782-9783 9828 9899-9901 9923-9924 9997-10009 10306 10531-10532 10607-10611 10876 11009 11123-11124 11609 11644-11648 11669-11671 11731-11734 11835-11836 12040-12041 12175-12176 12202-12205 12229-12230 12362 12434 12468-12469 12474 12565-12568 12573-12574 12642-

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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Salivary gland	Clontech	SALs03	981-985 8698-8700 11538-11540 14546-14549 20316 27814-27815 27989-27990 28424
skin fibroblast	ATCC	SFB001	1307 3374-3376 6285-6288 6791-6794 10306 12258 17026-17028 18029-18030 19011 19939 19972-19980 20182-20188 22141-22143 22160 22495 23415-23418 28424 30150-30156
skin fibroblast	ATCC	SFB002	2926 5805-5807 6166-6168 10306 12258 17026-17028 17038-17041 17455-17456 18029-18030 19011 19548-19553 19813 21060-21061 22141-22143 22160 22373 22495 22531-22533 26879 27636-27639 28424 30150-30156
skin fibroblast	ATCC	SFB003	5803-5804 6166-6168 12258 17335-17339 18029-18030 18778-18780 19062-19065 19548-19553 20182-20188 22007-22015 23051-23052 23419 25340-25341 27269-27270 27814-27815 28424 30150-30156
small intestine	Clontech	SIN001	83 87-94 195-200 307-308 332 373-374 557-559 674-675 783-784 852-855 901-904 1071 1240-1241 1470 1678-1680 1755-1762 1764-1766 1769-1772 2030 2048 2089-

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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			27600-27601 27814-27815 27819-27820 28142-28145 28233 29367 30141-30142
uterus	Clontech	UTR001	124-125 188-191 227-230 251-252 301 329-331 738-740 919-922 1028 1047 1453-1454 1562-1564 1705-1714 1893-1901 1912-1913 2366 2374-2377 2926 2988-2989 3001 3205-3207 4557-4560 4712-4713 4971-4974 5903-5906 5919-5921 6114-6136 6235-6237 6403-6404 6533-6535 6625-6626 6932-6938 7678-7680 7728 7771 7798-7801 7921-7923 7946 8010-8012 8084-8085 8090-8093 8137-8141 8313-8314 8368-8370 8415 8420-8421 8689-8690 9072-9074 9264-9265 9517-9521 9535-9537 9577-9578 9828-9832 9848-9850 9929-9935 9953 10033-10037 10268-10272 10508-10512 10537-10538 10980-10985 11071-11075 11135 11505-11506 11546 11609 11731-11734 11803-11804 12023-12026 12046-12049 12190-12191 12378-12397 12432-12433 12894-12897 13107-13117 13592-13597 13888-13895 13954-13956 14058-14059 14261-14263 14445-14447 14604 14650-14651 14988-14992 15182-15183 15187-15189 15290-15291 15390 15576-15577 15699-15700 15855-15857 16145-16146 16174-16176 16600 16643-16648 16716-16723 16851-16853 17330-17332 17454 17958-17962 18015-18016 18527 18655-18658 18673-18677 18761 18789 18825-18834 18894-18896 18899-18903 18936-18939 19036-19039 19074-19083 19362 19370 19375-19379 19387-19389 19442-19444 19560-19562 19609-19615 19693 19727-19732 19764-19767 19816-19818 19926-19929 19933-19937 19950 19981 20029-20043 20120 20122-20127 20146-20148 20151-20154 20289-20296 20298 20328-20330 20366-20368 20401-20405 20427-20431 20469-20471 20491-20494 20554-20557 20602-20606 20629-20630 20649-20652 20689-20692 20753 20758-20767 20801-20805 20858-20862 20864 20938-20942 21005-21008 21072-21075 21213-21215 21281-21294 21377-21397 21911-21912 21955-21957 21978-21982 22019-22025 22050-22055 22090-22091 22187-22192 22218-22224 22251-22252 22261-22264 22358-22359 22362-22364 22373 22405-22408 22571-22581 22622-22624 22644-22651 22663-22664 22887-22891 22955-22957 22969-22970 23047-23050 23094-23097 23141 23425-23427 23439-23447 23543-23544 24029-24033 24130-24144 25085-25090 25340-25341 25374-25375 25416-25417 26221-26223 26270-26272 26285-26290 26327 26607-26609 26676-26677 26755-26756 26853-26854 26860-26862 27173-27174 27294 27348-27353 27493-27496 27602-27606 27636-27639 27649-27654 27729-27739 27861-27864 27896-27927 28105-28121 28133-28137 28311-28313 28424 28426-28428 29339-29340 29378-29379 29962-29963 30150-30156

*The 16 tissue-mRNAs and their vendor source, are as follows: 1) Normal adult brain mRNA (Invitrogen), 2) normal adult kidney mRNA (Invitrogen), 3) normal adult liver mRNA (Invitrogen),

4) normal fetal brain mRNA (Invitrogen), 5) normal fetal kidney mRNA (Invitrogen), 6) normal fetal liver mRNA (Invitrogen), 7) normal fetal skin mRNA (Invitrogen), 8) human adrenal gland mRNA (Clontech), 9) human bone marrow mRNA (Clontech), 10) human leukemia lymphablastic mRNA (Clontech), 11) human thymus mRNA (Clontech), 12) human lymph node mRNA (Clontech), 13) human spinal cord mRNA (Clontech), 14) human thyroid mRNA (Clontech), 15) human esophagus mRNA (BioChain), 16) human conceptional umbilical cord mRNA (BioChain).

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
1	30369	C	1	23	76	
2	30370	B	2	1	735	
3	30371	B	3	1	783	
4	30372	B	4	104	266	
5	30373	B	5	1	1113	
6	30374	C	6	3	164	
7	30375	B	7	112	279	
8	30376	B	8	198	405	
9	30377	B	9	1	687	
10	30378	C	10	346	598	
11	30379	B	11	1	960	
12	30380	B	12	44	350	
13	30381	B	13	264	465	
14	30382	B	14	483	1556	
15	30383	B	15	140	838	
16	30384	B	16	1	372	
17	30385	B	17	1	1404	
18	30386	B	18	25	2013	
19	30387	C	19	1	381	
20	30388	C	20	605	755	
21	30389	B	21	1	912	
22	30390	C	22	124	315	
23	30391	C	23	44	310	
24	30392	B	24	1	330	
25	30393	B	25	1	411	
26	30394	B	26	147	257	
27	30395	B	27	1	597	
28	30396	B	28	201	862	
29	30397	C	29	249	515	
30	30398	B	30	41	816	
31	30399	C	31	26	142	
32	30400	B	32	259	2328	
33	30401	B	33	1	759	
34	30402	B	34	964	2121	
35	30403	C	35	298	449	
36	30404	C	36	115	396	
37	30405	C	37	148	318	
38	30406	C	38	383	483	
39	30407	B	39	1	1125	
40	30408	B	40	1	831	
41	30409	C	41	363	602	
42	30410	B	42	1	324	
43	30411	B	43	64	199	
44	30412	B	44	1	1007	
45	30413	C	45	380	583	
46	30414	B	46	1	432	
47	30415	C	47	1	249	
48	30416	B	48	1	798	
49	30417	B	49	14	1070	
50	30418	C	50	1	225	
51	30419	B	51	1	2673	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
52	30420	B	52	1	258	
53	30421	B	54	1	624	
54	30422	C	55	166	333	
55	30423	B	56	298	380	
56	30424	C	57	139	379	
57	30425	B	58	1	157	
58	30426	B	59	1	447	
59	30427	B	60	1	579	
60	30428	B	61	1	1059	
61	30429	B	62	1	816	
62	30430	B	63	1	558	
63	30431	B	64	1	540	
64	30432	B	65	1	555	
65	30433	B	66	1	648	
66	30434	B	67	1	798	
67	30435	B	68	1	1455	
68	30436	B	69	1	1278	
69	30437	B	70	88	3012	
70	30438	B	71	1	1092	
71	30439	B	72	575	1033	
72	30440	B	73	644	926	
73	30441	B	74	1	1239	
74	30442	B	75	1	1074	
75	30443	B	76	81	467	
76	30444	C	77	44	286	
77	30445	B	78	1	297	
78	30446	B	79	1	978	
79	30447	B	80	72	715	
80	30448	B	81	1	1296	
81	30449	B	82	63	162	
82	30450	C	83	22	420	
83	30451	C	84	201	733	
84	30452	C	85	417	575	
85	30453	B	86	1	267	
86	30454	B	87	112	738	
87	30455	C	88	260	379	
88	30456	B	89	77	399	
89	30457	B	90	158	420	
90	30458	B	91	1	1437	
91	30459	C	92	22	321	
92	30460	B	93	1	843	
93	30461	B	94	142	2798	
94	30462	B	95	887	8434	
95	30463	B	96	1	1014	
96	30464	B	97	1	1197	
97	30465	B	98	16	555	
98	30466	B	99	1	423	
99	30467	B	100	1	651	
100	30468	B	101	233	556	
101	30469	B	102	192	883	
102	30470	C	103	65	274	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
103	30471	C	104	328	546	
104	30472	B	105	80	3900	
105	30473	B	106	1	951	
106	30474	C	107	1	279	
107	30475	C	108	246	368	
108	30476	B	109	1	819	
109	30477	B	110	1	634	
110	30478	B	111	1	379	
111	30479	B	112	80	2747	
112	30480	C	113	139	414	
113	30481	C	114	1	330	
114	30482	B	115	53	618	
115	30483	B	116	1	426	
116	30484	C	117	135	296	
117	30485	C	118	239	432	
118	30486	C	119	381	776	
119	30487	B	120	1	381	
120	30488	C	121	42	175	
121	30489	C	122	1	399	
122	30490	B	123	1	792	
123	30491	B	124	1	894	
124	30492	B	125	1	3498	
125	30493	B	126	8	874	
126	30494	B	127	1	2160	
127	30495	B	128	1	1776	
128	30496	B	129	1	567	
129	30497	B	130	195	728	
130	30498	B	131	1	615	
131	30499	B	132	1	420	
132	30500	B	133	661	2711	
133	30501	B	134	1	621	
134	30502	C	136	1	465	
135	30503	C	137	113	502	
136	30504	C	139	78	269	
137	30505	C	140	98	472	
138	30506	B	141	403	533	
139	30507	C	142	64	315	
140	30508	B	143	1	591	
141	30509	C	144	528	1151	
142	30510	C	145	1	414	
143	30511	B	146	1	936	
144	30512	C	147	91	195	
145	30513	C	148	562	705	
146	30514	C	149	122	313	
147	30515	B	150	566	1535	
148	30516	C	151	75	248	
149	30517	C	152	1	624	
150	30518	C	153	551	655	
151	30519	C	154	315	497	
152	30520	C	155	262	554	
153	30521	C	156	1	282	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
154	30522	B	157	1	508	
155	30523	C	158	243	545	
156	30524	B	159	8	395	
157	30525	C	160	33	194	
158	30526	B	161	50	355	
159	30527	B	162	128	1230	
160	30528	B	163	243	710	
161	30529	B	164	121	742	
162	30530	B	165	152	227	
163	30531	C	166	156	503	
164	30532	B	167	67	1280	
165	30533	B	168	1	444	
166	30534	B	169	161	206	
167	30535	B	170	189	1207	
168	30536	B	171	1	613	
169	30537	B	172	1	70	
170	30538	C	173	611	751	
171	30539	B	174	398	2472	
172	30540	B	175	87	646	
173	30541	B	176	1	1455	
174	30542	C	177	1	339	
175	30543	B	178	1	1458	
176	30544	B	179	278	766	
177	30545	B	181	85	749	
178	30546	B	182	50	498	
179	30547	C	183	1	522	
180	30548	B	184	90	482	
181	30549	B	185	86	442	
182	30550	C	187	129	308	
183	30551	C	188	1	414	
184	30552	B	190	1	378	
185	30553	C	192	252	308	
186	30554	B	193	1	576	
187	30555	C	194	1093	1311	
188	30556	B	195	45	324	
189	30557	B	196	1	249	
190	30558	C	197	309	443	
191	30559	C	198	615	866	
192	30560	B	199	86	1332	
193	30561	B	200	49	334	
194	30562	B	201	64	638	
195	30563	C	202	195	338	
196	30564	C	203	1	357	
197	30565	B	204	1	693	
198	30566	C	205	121	291	
199	30567	C	206	156	380	
200	30568	C	207	1211	1456	
201	30569	B	208	62	328	
202	30570	C	209	105	179	
203	30571	B	210	229	1483	
204	30572	B	211	1	749	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Met hod	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
205	30573	B	212	1	190	
206	30574	C	213	121	367	
207	30575	B	214	121	456	
208	30576	B	215	1	2631	
209	30577	B	216	63	419	
210	30578	B	217	114	485	
211	30579	B	218	628	1447	
212	30580	C	219	252	377	
213	30581	B	220	1	847	
214	30582	B	221	68	343	
215	30583	B	222	138	911	
216	30584	B	223	44	882	
217	30585	B	224	1	429	
218	30586	B	225	87	312	
219	30587	C	226	44	343	
220	30588	C	227	41	286	
221	30589	C	228	1145	1372	
222	30590	B	229	1	720	
223	30591	C	230	1	430	
224	30592	C	231	58	297	
225	30593	B	232	613	683	
226	30594	B	233	613	683	
227	30595	C	234	238	455	
228	30596	B	235	319	615	
229	30597	C	236	255	494	
230	30598	B	237	106	600	
231	30599	B	238	1	654	
232	30600	B	239	1	654	
233	30601	B	240	243	356	
234	30602	B	241	1	932	
235	30603	C	242	36	215	
236	30604	B	243	1	288	
237	30605	C	244	25	186	
238	30606	B	245	1	574	
239	30607	B	246	1	1257	
240	30608	B	247	162	263	
241	30609	C	248	79	207	
242	30610	B	249	194	276	
243	30611	B	250	1	1671	
244	30612	C	251	118	311	
245	30613	B	252	88	1485	
246	30614	B	253	339	443	
247	30615	B	254	667	1165	
248	30616	B	255	1	981	
249	30617	B	256	450	3131	
250	30618	B	257	900	1199	
251	30619	C	258	5	271	
252	30620	B	259	65	689	
253	30621	C	260	1	321	
254	30622	B	261	1	137	
255	30623	B	262	34	282	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
256	30624	B	263	46	856	
257	30625	C	264	157	468	
258	30626	B	265	148	403	
259	30627	C	266	248	481	
260	30628	B	267	171	393	
261	30629	B	268	1	1078	
262	30630	B	269	1	550	
263	30631	B	270	1	1455	
264	30632	B	271	171	602	
265	30633	B	272	1	1056	
266	30634	B	273	1	1101	
267	30635	B	274	1	2335	
268	30636	B	275	303	419	
269	30637	B	276	1	615	
270	30638	B	277	1	543	
271	30639	B	278	1	1602	
272	30640	C	279	585	1001	
273	30641	C	280	260	379	
274	30642	B	281	1	1437	
275	30643	C	282	22	321	
276	30644	B	283	1	843	
277	30645	B	284	142	2796	
278	30646	B	285	458	7217	
279	30647	B	286	84	186	
280	30648	C	287	67	229	
281	30649	C	288	15	245	
282	30650	C	289	125	232	
283	30651	B	290	1	594	
284	30652	B	291	376	670	
285	30653	C	292	82	405	
286	30654	B	293	35	651	
287	30655	B	294	56	487	
288	30656	C	295	313	498	
289	30657	C	296	118	261	
290	30658	B	297	198	1868	
291	30659	B	298	1	1665	
292	30660	C	299	73	108	
293	30661	B	300	1	408	
294	30662	B	301	1	444	
295	30663	B	302	8	311	
296	30664	C	303	144	350	
297	30665	B	304	1	669	
298	30666	C	305	416	820	
299	30667	B	306	253	837	
300	30668	B	307	44	475	
301	30669	B	308	185	885	
302	30670	C	309	206	337	
303	30671	B	310	1	393	
304	30672	B	311	1	1259	
305	30673	B	312	24	434	
306	30674	B	313	44	2687	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
307	30675	B	314	1	154	
308	30676	B	315	288	770	
309	30677	B	316	85	683	
310	30678	B	317	1	873	
311	30679	B	318	1	1737	
312	30680	C	319	1	690	
313	30681	B	320	58	1487	
314	30682	B	321	1	816	
315	30683	B	322	25	772	
316	30684	B	323	42	271	
317	30685	C	324	16	159	
318	30686	C	325	74	280	
319	30687	C	326	221	545	
320	30688	B	327	192	364	
321	30689	C	328	390	638	
322	30690	B	329	151	4215	
323	30691	B	330	1	2076	
324	30692	B	331	1	465	
325	30693	B	332	40	1350	
326	30694	B	333	1	489	
327	30695	B	334	285	744	
328	30696	C	335	96	347	
329	30697	C	336	213	326	
330	30698	B	337	776	4384	
331	30699	B	338	201	317	
332	30700	B	339	1	2713	
333	30701	B	340	1	894	
334	30702	B	341	1	3842	
335	30703	C	342	745	1131	
336	30704	B	343	82	411	
337	30705	B	344	126	2123	
338	30706	B	345	57	1641	
339	30707	C	346	211	654	
340	30708	B	347	44	266	
341	30709	B	348	1	927	
342	30710	C	349	20	124	
343	30711	C	350	9	455	
344	30712	C	351	188	304	
345	30713	C	352	1	333	
346	30714	C	353	140	298	
347	30715	B	354	73	2171	
348	30716	B	355	1	1374	
349	30717	B	356	150	398	
350	30718	B	357	1	585	
351	30719	B	358	1	1716	
352	30720	B	359	81	1912	
353	30721	B	360	249	770	
354	30722	B	361	474	2875	
355	30723	C	362	1	483	
356	30724	C	363	1	251	
357	30725	C	364	28	407	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
358	30726	C	365	88	204	
359	30727	B	366	474	684	
360	30728	C	367	41	394	
361	30729	B	368	253	1044	
362	30730	B	369	468	1111	
363	30731	B	370	1	558	
364	30732	B	371	21	345	
365	30733	B	372	1	744	
366	30734	B	373	1	795	
367	30735	B	374	1	685	
368	30736	B	375	94	414	
369	30737	C	376	86	268	
370	30738	B	377	1	1003	
371	30739	B	378	41	1385	
372	30740	B	379	1	510	
373	30741	B	380	40	746	
374	30742	B	381	100	1991	
375	30743	B	382	1	267	
376	30744	C	383	168	278	
377	30745	C	384	173	208	
378	30746	B	385	141	4538	
379	30747	B	386	1	4086	
380	30748	C	387	398	474	
381	30749	B	388	1	762	
382	30750	B	389	1	1584	
383	30751	B	390	1	2703	
384	30752	B	391	1	489	
385	30753	B	392	527	780	
386	30754	B	393	1	4050	
387	30755	B	394	859	2958	
388	30756	B	395	639	2307	
389	30757	B	396	1	642	
390	30758	B	397	1	3639	
391	30759	B	398	219	540	
392	30760	B	399	1	3225	
393	30761	B	400	1	7552	
394	30762	C	401	626	1201	
395	30763	C	402	627	827	
396	30764	C	403	1	243	
397	30765	B	404	335	538	
398	30766	B	405	41	409	
399	30767	B	406	160	540	
400	30768	B	407	1	597	
401	30769	B	408	1	1605	
402	30770	B	409	1	351	
403	30771	B	410	65	601	
404	30772	B	411	1	870	
405	30773	B	412	91	2867	
406	30774	B	413	33	410	
407	30775	B	414	298	343	
408	30776	B	415	70	310	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
409	30777	B	416	64	1929	
410	30778	B	417	1	298	
411	30779	B	418	37	2612	
412	30780	B	419	1	510	
413	30781	B	420	44	1111	
414	30782	B	421	26	175	
415	30783	C	422	7	57	
416	30784	C	423	27	230	
417	30785	C	424	7	144	
418	30786	B	425	1	1746	
419	30787	C	426	318	486	
420	30788	B	427	896	1115	
421	30789	C	428	106	309	
422	30790	C	429	52	402	
423	30791	B	430	1	309	
424	30792	B	431	167	492	
425	30793	C	432	144	296	
426	30794	B	433	1	786	
427	30795	B	434	336	1303	
428	30796	B	435	333	419	
429	30797	B	436	1	489	
430	30798	C	437	1	199	
431	30799	C	438	110	239	
432	30800	C	439	175	303	
433	30801	C	440	35	181	
434	30802	B	441	1	1896	
435	30803	C	442	1	331	
436	30804	C	443	71	344	
437	30805	C	444	25	135	
438	30806	C	445	406	595	
439	30807	C	446	148	228	
440	30808	C	447	80	106	
441	30809	C	448	7	375	
442	30810	C	449	300	437	
443	30811	C	450	1	357	
444	30812	B	451	1	729	
445	30813	B	452	58	1287	
446	30814	C	453	1	410	
447	30815	C	454	1	411	
448	30816	C	455	1	420	
449	30817	B	456	1	555	
450	30818	B	457	376	1035	
451	30819	B	458	678	807	
452	30820	B	459	88	1485	
453	30821	B	460	300	2082	
454	30822	B	461	1	819	
455	30823	B	462	780	998	
456	30824	B	463	1	1871	
457	30825	B	464	1	1703	
458	30826	B	465	1	594	
459	30827	C	466	120	245	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
460	30828	C	467	1	387	
461	30829	B	468	1	1678	
462	30830	B	469	1	533	
463	30831	B	470	347	656	
464	30832	B	471	1	1098	
465	30833	B	472	224	1518	
466	30834	C	473	44	244	
467	30835	B	474	1	1251	
468	30836	B	475	1	428	
469	30837	B	476	1	495	
470	30838	C	477	233	373	
471	30839	B	478	8	950	
472	30840	C	479	1	813	
473	30841	B	480	1	1071	
474	30842	C	481	224	418	
475	30843	B	482	39	851	
476	30844	B	483	1	2006	
477	30845	B	484	1	561	
478	30846	B	485	167	227	
479	30847	B	486	1	777	
480	30848	B	487	1	645	
481	30849	B	488	1	1749	
482	30850	C	489	26	847	
483	30851	C	490	243	392	
484	30852	C	491	303	407	
485	30853	C	492	23	300	
486	30854	B	493	131	336	
487	30855	C	494	64	156	
488	30856	B	495	180	712	
489	30857	B	496	1	1104	
490	30858	B	497	24	917	
491	30859	B	498	65	228	
492	30860	B	499	1	2172	
493	30861	B	500	1	1338	
494	30862	B	501	1	795	
495	30863	C	502	181	410	
496	30864	B	503	69	1322	
497	30865	B	504	531	1315	
498	30866	C	505	24	320	
499	30867	B	506	1	791	
500	30868	B	507	1	3256	
501	30869	C	508	361	549	
502	30870	B	509	729	3252	
503	30871	B	510	424	1710	
504	30872	C	511	247	750	
505	30873	B	512	11	124	
506	30874	B	514	116	1079	
507	30875	B	515	1	766	
508	30876	B	516	185	796	
509	30877	B	517	1	456	
510	30878	B	518	99	435	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
511	30879	B	519	1	834	
512	30880	B	520	54	246	
513	30881	B	521	1	372	
514	30882	C	522	78	305	
515	30883	C	523	329	484	
516	30884	B	524	1	459	
517	30885	B	525	630	889	
518	30886	B	526	95	343	
519	30887	B	527	353	610	
520	30888	B	528	113	529	
521	30889	B	529	362	1400	
522	30890	B	530	1	441	
523	30891	C	531	1	327	
524	30892	B	532	1	909	
525	30893	B	534	669	1268	
526	30894	B	535	293	826	
527	30895	C	536	12	155	
528	30896	C	537	1488	1706	
529	30897	C	538	26	211	
530	30898	C	539	30	185	
531	30899	B	540	1	789	
532	30900	B	541	63	358	
533	30901	B	542	1	900	
534	30902	B	543	1	728	
535	30903	B	544	112	220	
536	30904	B	545	49	386	
537	30905	B	546	1	585	
538	30906	B	547	328	531	
539	30907	B	548	10	987	
540	30908	B	549	49	248	
541	30909	B	550	131	368	
542	30910	B	551	80	1098	
543	30911	B	552	1	1364	
544	30912	B	553	1	1294	
545	30913	B	554	1	1995	
546	30914	B	555	1	279	
547	30915	B	556	175	715	
548	30916	B	557	1	636	
549	30917	B	558	1331	1600	
550	30918	B	559	32	406	
551	30919	B	560	38	206	
552	30920	B	561	1	1266	
553	30921	C	562	359	501	
554	30922	B	563	315	465	
555	30923	B	564	94	1683	
556	30924	B	565	1	1570	
557	30925	B	566	139	1734	
558	30926	B	567	1	810	
559	30927	B	568	658	1548	
560	30928	B	569	9	395	
561	30929	B	570	1	567	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
562	30930	B	571	1	567	
563	30931	B	572	1	789	
564	30932	B	573	49	3187	
565	30933	B	574	1	1824	
566	30934	B	575	49	1413	
567	30935	B	576	1	1572	
568	30936	C	577	372	468	
569	30937	C	578	58	225	
570	30938	B	579	79	299	
571	30939	B	580	1	645	
572	30940	C	581	582	749	
573	30941	B	582	170	463	
574	30942	B	583	311	520	
575	30943	B	584	1	1074	
576	30944	B	585	39	140	
577	30945	B	586	60	1685	
578	30946	B	587	106	879	
579	30947	C	588	67	362	
580	30948	B	589	45	126	
581	30949	C	590	1	390	
582	30950	C	591	49	240	
583	30951	B	592	1	496	
584	30952	B	593	94	482	
585	30953	C	594	12	341	
586	30954	B	595	1	354	
587	30955	B	596	1	711	
588	30956	B	597	123	412	
589	30957	B	598	1	1107	
590	30958	B	599	1	800	
591	30959	C	600	82	408	
592	30960	B	601	1	3174	
593	30961	B	602	1	444	
594	30962	B	603	1	1671	
595	30963	B	604	1	603	
596	30964	B	605	339	443	
597	30965	C	606	237	380	
598	30966	B	607	1	771	
599	30967	B	608	1	1767	
600	30968	C	609	1	801	
601	30969	B	610	1	1062	
602	30970	B	611	450	3131	
603	30971	C	612	178	435	
604	30972	C	613	164	319	
605	30973	C	614	1	385	
606	30974	C	615	392	853	
607	30975	C	616	24	200	
608	30976	C	617	34	327	
609	30977	B	618	1	624	
610	30978	B	619	179	1222	
611	30979	B	620	1	916	
612	30980	B	621	151	339	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
613	30981	B	622	135	218	
614	30982	B	623	126	300	
615	30983	C	624	258	467	
616	30984	B	625	58	1038	
617	30985	B	626	246	4677	
618	30986	B	627	1	583	
619	30987	C	628	65	283	
620	30988	B	629	162	909	
621	30989	B	630	1	1062	
622	30990	B	631	1	909	
623	30991	C	632	160	297	
624	30992	B	633	352	1143	
625	30993	C	634	301	459	
626	30994	B	635	1	906	
627	30995	B	636	1	654	
628	30996	B	637	1	528	
629	30997	B	638	1	1102	
630	30998	C	639	81	299	
631	30999	B	640	1	345	
632	31000	B	641	39	360	
633	31001	B	642	22	293	
634	31002	C	643	1	504	
635	31003	B	644	107	3786	
636	31004	B	645	1	576	
637	31005	B	646	66	152	
638	31006	B	647	226	522	
639	31007	B	648	1	49	
640	31008	C	649	50	172	
641	31009	C	650	1	516	
642	31010	B	651	1	615	
643	31011	B	652	1	495	
644	31012	B	653	1	663	
645	31013	B	654	1	1812	
646	31014	B	655	1	1401	
647	31015	B	656	102	1151	
648	31016	B	657	1	385	
649	31017	B	658	232	987	
650	31018	B	659	1	1221	
651	31019	B	660	296	496	
652	31020	B	661	57	285	
653	31021	C	662	203	271	
654	31022	B	663	1	711	
655	31023	C	664	351	542	
656	31024	C	665	420	695	
657	31025	B	666	1	1860	
658	31026	B	667	71	2167	
659	31027	B	668	6	344	
660	31028	B	669	217	693	
661	31029	C	670	1	417	
662	31030	B	671	1	990	
663	31031	B	672	109	1169	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
664	31032	C	673	40	117	
665	31033	C	674	301	560	
666	31034	B	675	1	396	
667	31035	B	676	483	1033	
668	31036	B	677	673	3407	
669	31037	B	678	4	672	
670	31038	C	679	39	116	
671	31039	B	680	1	459	
672	31040	B	681	19	370	
673	31041	B	682	112	704	
674	31042	C	683	387	578	
675	31043	B	684	175	254	
676	31044	B	685	1	501	
677	31045	B	686	290	389	
678	31046	B	687	1	486	
679	31047	B	688	1	651	
680	31048	B	689	181	401	
681	31049	B	690	117	406	
682	31050	B	691	1	169	
683	31051	B	692	1	1539	
684	31052	B	693	1	475	
685	31053	B	694	1	1575	
686	31054	B	695	1	507	
687	31055	B	696	1	498	
688	31056	C	697	253	492	
689	31057	B	698	1	588	
690	31058	B	699	75	291	
691	31059	B	700	1	1355	
692	31060	B	701	112	259	
693	31061	C	702	492	833	
694	31062	B	703	297	483	
695	31063	B	704	45	471	
696	31064	C	705	175	318	
697	31065	B	706	1	1074	
698	31066	B	707	94	1180	
699	31067	B	708	1	3866	
700	31068	C	709	215	424	
701	31069	B	710	1	499	
702	31070	B	711	210	325	
703	31071	B	712	1	786	
704	31072	B	713	1	777	
705	31073	B	714	174	1804	
706	31074	B	715	17	368	
707	31075	B	716	769	1831	
708	31076	B	717	76	301	
709	31077	B	718	1	825	
710	31078	C	719	1	396	
711	31079	B	720	93	2449	
712	31080	B	721	408	687	
713	31081	B	722	97	662	
714	31082	B	723	169	610	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
715	31083	B	724	1	2511	
716	31084	C	725	104	410	
717	31085	C	726	75	527	
718	31086	C	727	7	263	
719	31087	B	728	40	1725	
720	31088	B	729	290	1671	
721	31089	B	730	46	465	
722	31090	C	731	378	644	
723	31091	B	732	48	2331	
724	31092	B	733	1	738	
725	31093	B	734	1	1051	
726	31094	B	735	1	840	
727	31095	C	736	291	551	
728	31096	B	737	1	1308	
729	31097	B	738	1	291	
730	31098	C	739	1	702	
731	31099	B	740	1	379	
732	31100	B	741	80	2747	
733	31101	B	742	1	1992	
734	31102	B	743	293	1296	
735	31103	C	744	769	1017	
736	31104	C	745	166	294	
737	31105	B	746	928	1483	
738	31106	B	747	247	375	
739	31107	C	748	47	582	
740	31108	B	749	47	388	
741	31109	B	750	53	458	
742	31110	C	751	32	277	
743	31111	B	752	1	1641	
744	31112	C	753	1	483	
745	31113	B	754	1	1518	
746	31114	B	755	1	321	
747	31115	C	756	604	779	
748	31116	B	757	695	967	
749	31117	B	758	1	768	
750	31118	B	759	101	531	
751	31119	B	760	1	1014	
752	31120	C	761	424	564	
753	31121	B	762	1	333	
754	31122	B	763	15	165	
755	31123	B	764	1	555	
756	31124	B	765	344	476	
757	31125	B	766	1	648	
758	31126	B	767	1	981	
759	31127	C	768	22	162	
760	31128	B	769	1	225	
761	31129	B	770	232	1671	
762	31130	B	771	166	504	
763	31131	B	772	473	1694	
764	31132	C	773	232	414	
765	31133	C	774	374	463	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
766	31134	B	775	1	1128	
767	31135	B	776	337	1284	
768	31136	C	777	25	282	
769	31137	C	778	4	63	
770	31138	C	779	496	1041	
771	31139	C	780	234	365	
772	31140	B	781	1	669	
773	31141	B	782	228	305	
774	31142	B	783	102	755	
775	31143	B	784	1	465	
776	31144	B	785	45	336	
777	31145	C	786	220	366	
778	31146	B	787	332	456	
779	31147	B	788	169	450	
780	31148	B	789	1	1173	
781	31149	B	790	36	355	
782	31150	C	791	354	482	
783	31151	C	792	328	708	
784	31152	B	793	1	829	
785	31153	B	794	14	182	
786	31154	B	795	307	1412	
787	31155	C	796	3	332	
788	31156	B	797	57	704	
789	31157	B	798	1	2406	
790	31158	C	799	1	759	
791	31159	B	800	1	351	
792	31160	B	801	142	272	
793	31161	B	802	34	2951	
794	31162	B	803	92	994	
795	31163	B	804	115	1746	
796	31164	C	805	292	408	
797	31165	B	806	1	880	
798	31166	C	807	156	329	
799	31167	C	808	119	328	
800	31168	C	809	1	492	
801	31169	B	810	1	516	
802	31170	B	811	1	624	
803	31171	B	812	24	1868	
804	31172	C	813	164	208	
805	31173	C	814	91	249	
806	31174	B	815	1	1059	
807	31175	C	816	80	106	
808	31176	C	817	283	408	
809	31177	C	818	1	357	
810	31178	C	819	1	909	
811	31179	B	820	26	71	
812	31180	B	821	1	714	
813	31181	B	822	1	678	
814	31182	B	823	1	675	
815	31183	B	824	24	1046	
816	31184	B	825	1	933	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Met hod	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
817	31185	B	826	1	363	
818	31186	B	827	112	1655	
819	31187	B	828	1	417	
820	31188	B	829	88	1485	
821	31189	C	830	1	411	
822	31190	B	831	114	277	
823	31191	C	832	671	1039	
824	31192	B	833	63	342	
825	31193	B	834	3530	4798	
826	31194	B	835	1	333	
827	31195	B	836	1	831	
828	31196	B	837	1	2514	
829	31197	B	838	98	250	
830	31198	B	839	1	5247	
831	31199	B	840	1	531	
832	31200	B	841	167	466	
833	31201	B	842	160	417	
834	31202	B	843	215	380	
835	31203	B	844	706	1262	
836	31204	B	845	41	368	
837	31205	C	846	252	578	
838	31206	C	847	18	380	
839	31207	C	848	14	349	
840	31208	B	849	1	1176	
841	31209	B	850	244	1174	
842	31210	C	851	27	146	
843	31211	B	852	217	1866	
844	31212	B	853	98	242	
845	31213	B	854	52	2112	
846	31214	B	855	98	242	
847	31215	C	856	237	518	
848	31216	C	857	1	528	
849	31217	C	858	213	365	
850	31218	B	859	86	478	
851	31219	B	860	1	903	
852	31220	B	861	191	539	
853	31221	C	862	283	480	
854	31222	B	863	248	738	
855	31223	B	864	7	1602	
856	31224	B	865	113	375	
857	31225	B	866	50	435	
858	31226	B	867	50	646	
859	31227	B	868	1	2292	
860	31228	B	869	1	2385	
861	31229	B	870	184	852	
862	31230	B	871	1	408	
863	31231	B	872	218	484	
864	31232	B	873	90	588	
865	31233	B	874	445	625	
866	31234	B	875	138	618	
867	31235	B	876	1	753	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
868	31236	B	877	1	489	
869	31237	B	878	113	366	
870	31238	C	879	271	489	
871	31239	B	880	918	3257	
872	31240	B	881	185	631	
873	31241	C	882	3	194	
874	31242	B	883	80	3219	
875	31243	B	884	213	1835	
876	31244	C	885	132	224	
877	31245	B	886	1	741	
878	31246	C	887	132	224	
879	31247	B	888	1	1281	
880	31248	B	889	125	1910	
881	31249	B	890	1	1449	
882	31250	B	891	284	696	
883	31251	B	892	139	390	
884	31252	B	893	1	1308	
885	31253	B	894	1	594	
886	31254	B	895	1	678	
887	31255	B	896	19	240	
888	31256	B	897	47	330	
889	31257	B	898	1	388	
890	31258	B	899	52	564	
891	31259	C	900	310	672	
892	31260	B	901	1	1338	
893	31261	C	902	77	214	
894	31262	C	903	213	467	
895	31263	C	904	202	426	
896	31264	B	905	68	567	
897	31265	C	906	32	205	
898	31266	C	907	513	701	
899	31267	B	908	1	1083	
900	31268	B	909	787	1633	
901	31269	C	910	40	288	
902	31270	B	911	178	330	
903	31271	B	912	129	520	
904	31272	B	913	2267	2626	
905	31273	C	914	34	87	
906	31274	B	915	23	610	
907	31275	B	916	1	1011	
908	31276	B	917	1	156	
909	31277	B	918	1	754	
910	31278	B	919	1	679	
911	31279	B	920	149	761	
912	31280	B	921	38	1175	
913	31281	C	922	542	724	
914	31282	B	923	31	283	
915	31283	B	924	21	341	
916	31284	B	925	199	361	
917	31285	B	926	293	427	
918	31286	B	927	56	145	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
919	31287	B	928	21	341	
920	31288	B	929	199	361	
921	31289	B	930	293	427	
922	31290	B	931	305	465	
923	31291	B	932	280	457	
924	31292	C	933	45	562	
925	31293	B	934	130	618	
926	31294	B	935	418	1620	
927	31295	B	936	115	252	
928	31296	B	937	1	573	
929	31297	B	938	1	2661	
930	31298	B	939	1	1345	
931	31299	C	940	747	1220	
932	31300	C	941	249	429	
933	31301	B	942	1	363	
934	31302	C	943	390	589	
935	31303	B	944	437	1553	
936	31304	B	945	1	1521	
937	31305	C	946	84	347	
938	31306	B	949	80	315	
939	31307	B	950	1	537	
940	31308	C	951	181	330	
941	31309	C	952	55	123	
942	31310	C	953	52	195	
943	31311	C	954	55	123	
944	31312	B	955	336	648	
945	31313	B	956	1	894	
946	31314	B	957	239	1008	
947	31315	B	958	126	308	
948	31316	B	959	1	747	
949	31317	B	960	101	351	
950	31318	B	961	179	1161	
951	31319	B	962	1	138	
952	31320	B	963	8	791	
953	31321	C	964	218	358	
954	31322	C	965	155	454	
955	31323	C	966	124	303	
956	31324	C	967	1	246	
957	31325	B	968	208	364	
958	31326	C	969	95	256	
959	31327	C	970	312	467	
960	31328	B	971	92	424	
961	31329	B	972	88	147	
962	31330	C	973	434	775	
963	31331	B	974	26	1781	
964	31332	C	975	363	692	
965	31333	B	976	201	563	
966	31334	B	977	348	687	
967	31335	C	978	529	660	
968	31336	C	979	418	738	
969	31337	C	980	25	177	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
970	31338	B	981	308	388	
971	31339	C	982	230	580	
972	31340	B	983	101	342	
973	31341	B	984	1	2341	
974	31342	C	985	1	642	
975	31343	B	986	1	1173	
976	31344	B	987	39	6743	
977	31345	B	988	1	516	
978	31346	B	989	1	756	
979	31347	B	990	1	912	
980	31348	B	991	310	441	
981	31349	C	992	58	300	
982	31350	B	993	80	1344	
983	31351	C	994	325	414	
984	31352	B	995	80	1582	
985	31353	C	996	143	499	
986	31354	B	997	173	375	
987	31355	C	998	126	268	
988	31356	B	999	1	762	
989	31357	B	1000	1	642	
990	31358	B	1001	1	1980	
991	31359	B	1002	67	456	
992	31360	B	1003	48	335	
993	31361	B	1004	1	1251	
994	31362	B	1005	1	642	
995	31363	B	1006	1	570	
996	31364	C	1007	1	687	
997	31365	B	1008	1	5450	
998	31366	B	1009	586	852	
999	31367	B	1010	299	530	
1000	31368	B	1011	1	1659	
1001	31369	B	1012	2	550	
1002	31370	C	1013	2	97	
1003	31371	B	1014	1114	1476	
1004	31372	B	1015	22	822	
1005	31373	C	1016	646	903	
1006	31374	C	1017	1	351	
1007	31375	B	1018	226	1284	
1008	31376	B	1019	138	997	
1009	31377	B	1020	341	527	
1010	31378	B	1021	157	1415	
1011	31379	B	1022	55	211	
1012	31380	B	1023	55	211	
1013	31381	C	1024	18	197	
1014	31382	B	1025	1	876	
1015	31383	B	1026	276	487	
1016	31384	B	1027	1	294	
1017	31385	B	1028	273	377	
1018	31386	B	1029	1	936	
1019	31387	B	1030	1	1158	
1020	31388	C	1031	104	283	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Met hod	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
1021	31389	B	1032	1	720	
1022	31390	B	1033	1	219	
1023	31391	B	1034	1	170	
1024	31392	B	1035	300	831	
1025	31393	C	1036	1	456	
1026	31394	B	1037	1	1149	
1027	31395	B	1038	1	627	
1028	31396	B	1039	161	375	
1029	31397	B	1040	1	360	
1030	31398	B	1041	1	549	
1031	31399	B	1042	1	384	
1032	31400	B	1046	1	675	
1033	31401	C	1047	379	675	
1034	31402	B	1048	166	388	
1035	31403	B	1049	26	66	
1036	31404	B	1050	1	897	
1037	31405	B	1051	30	1359	
1038	31406	B	1052	1	990	
1039	31407	B	1053	52	1507	
1040	31408	C	1054	66	290	
1041	31409	B	1055	158	2072	
1042	31410	B	1056	1	654	
1043	31411	B	1057	51	1143	
1044	31412	C	1058	66	290	
1045	31413	B	1059	547	1510	
1046	31414	B	1060	1	1499	
1047	31415	B	1061	1	3347	
1048	31416	C	1062	116	235	
1049	31417	B	1063	1	1185	
1050	31418	C	1064	221	823	
1051	31419	B	1065	235	359	
1052	31420	C	1066	1	360	
1053	31421	B	1067	49	386	
1054	31422	C	1068	63	383	
1055	31423	B	1069	60	213	
1056	31424	B	1070	1	919	
1057	31425	B	1071	294	557	
1058	31426	B	1072	1	486	
1059	31427	B	1073	1	450	
1060	31428	C	1074	28	207	
1061	31429	B	1075	1	585	
1062	31430	B	1076	60	213	
1063	31431	B	1077	18	457	
1064	31432	B	1078	112	177	
1065	31433	C	1079	1	375	
1066	31434	B	1080	39	91	
1067	31435	B	1081	91	237	
1068	31436	B	1082	255	376	
1069	31437	B	1083	18	431	
1070	31438	B	1084	98	552	
1071	31439	B	1085	1679	1964	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
1072	31440	B	1086	132	1200	
1073	31441	B	1087	95	418	
1074	31442	B	1088	26	56	
1075	31443	B	1089	1	873	
1076	31444	C	1090	107	196	
1077	31445	B	1091	157	777	
1078	31446	B	1092	1	1273	
1079	31447	B	1093	1	202	
1080	31448	B	1094	1	382	
1081	31449	C	1095	189	449	
1082	31450	C	1096	325	429	
1083	31451	C	1097	3	80	
1084	31452	B	1098	50	691	
1085	31453	B	1099	1	474	
1086	31454	B	1100	3	335	
1087	31455	B	1101	137	617	
1088	31456	C	1102	69	134	
1089	31457	B	1103	369	886	
1090	31458	B	1104	1	1332	
1091	31459	B	1105	106	584	
1092	31460	C	1106	97	420	
1093	31461	C	1107	142	381	
1094	31462	B	1108	214	2544	
1095	31463	B	1109	238	1323	
1096	31464	B	1110	1	3000	
1097	31465	B	1111	203	313	
1098	31466	B	1112	288	375	
1099	31467	B	1113	1	480	
1100	31468	C	1114	286	351	
1101	31469	B	1115	59	376	
1102	31470	C	1116	287	504	
1103	31471	B	1117	878	2032	
1104	31472	B	1118	52	648	
1105	31473	B	1119	1	207	
1106	31474	C	1120	1	492	
1107	31475	B	1121	46	830	
1108	31476	B	1122	1	525	
1109	31477	B	1123	1	930	
1110	31478	C	1124	157	606	
1111	31479	C	1125	70	405	
1112	31480	C	1126	247	411	
1113	31481	C	1127	339	590	
1114	31482	B	1128	1	1881	
1115	31483	C	1129	258	452	
1116	31484	B	1130	241	733	
1117	31485	C	1131	294	530	
1118	31486	B	1132	1	439	
1119	31487	B	1133	16	612	
1120	31488	C	1134	234	377	
1121	31489	B	1135	134	763	
1122	31490	C	1136	1	228	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
1123	31491	B	1137	63	443	
1124	31492	C	1138	30	269	
1125	31493	B	1139	44	151	
1126	31494	B	1140	69	199	
1127	31495	B	1141	347	2830	
1128	31496	B	1142	1	576	
1129	31497	C	1143	49	129	
1130	31498	B	1144	1	1107	
1131	31499	B	1145	17	153	
1132	31500	B	1146	277	694	
1133	31501	B	1147	1	735	
1134	31502	B	1148	1	1110	
1135	31503	B	1149	55	552	
1136	31504	C	1150	463	591	
1137	31505	B	1151	136	266	
1138	31506	B	1152	1	795	
1139	31507	B	1153	128	880	
1140	31508	C	1154	178	366	
1141	31509	B	1155	1	654	
1142	31510	B	1156	1	3294	
1143	31511	B	1157	16	854	
1144	31512	B	1158	1093	1185	
1145	31513	B	1159	1	930	
1146	31514	B	1160	1	3969	
1147	31515	B	1161	1	4173	
1148	31516	B	1162	1	2187	
1149	31517	B	1163	47	993	
1150	31518	B	1164	1	1241	
1151	31519	B	1165	46	2170	
1152	31520	B	1166	1	1781	
1153	31521	B	1167	179	583	
1154	31522	C	1168	167	442	
1155	31523	B	1169	44	1848	
1156	31524	C	1170	1	417	
1157	31525	B	1171	1	198	
1158	31526	B	1172	231	452	
1159	31527	B	1173	219	326	
1160	31528	B	1174	212	302	
1161	31529	B	1175	748	1084	
1162	31530	B	1176	1	540	
1163	31531	C	1177	21	143	
1164	31532	B	1178	76	1300	
1165	31533	B	1179	1	1324	
1166	31534	B	1180	1	1065	
1167	31535	B	1181	1	1263	
1168	31536	B	1182	1	1809	
1169	31537	B	1183	10	406	
1170	31538	B	1184	65	287	
1171	31539	B	1185	25	337	
1172	31540	B	1186	59	698	
1173	31541	C	1187	329	527	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
1174	31542	B	1188	1	1068	
1175	31543	B	1189	72	330	
1176	31544	B	1190	14	239	
1177	31545	B	1191	1	919	
1178	31546	B	1192	462	786	
1179	31547	B	1193	1	3468	
1180	31548	B	1194	16	457	
1181	31549	B	1195	1	697	
1182	31550	C	1196	1	145	
1183	31551	B	1197	91	450	
1184	31552	B	1198	1	1050	
1185	31553	B	1199	101	428	
1186	31554	B	1200	41	205	
1187	31555	B	1201	358	1082	
1188	31556	B	1202	1	183	
1189	31557	B	1203	1	1053	
1190	31558	B	1204	73	336	
1191	31559	B	1205	553	1587	
1192	31560	C	1206	118	366	
1193	31561	B	1207	1	423	
1194	31562	B	1208	120	338	
1195	31563	B	1209	1	1665	
1196	31564	B	1210	1	639	
1197	31565	B	1211	1	660	
1198	31566	B	1212	11	434	
1199	31567	B	1213	1	567	
1200	31568	B	1214	1	801	
1201	31569	C	1215	56	177	
1202	31570	B	1216	439	678	
1203	31571	B	1217	20	201	
1204	31572	B	1218	74	267	
1205	31573	B	1219	74	325	
1206	31574	B	1220	37	340	
1207	31575	B	1221	1	588	
1208	31576	B	1222	136	294	
1209	31577	B	1223	238	392	
1210	31578	B	1224	109	1394	
1211	31579	C	1225	300	653	
1212	31580	B	1226	32	3327	
1213	31581	B	1227	497	1306	
1214	31582	C	1228	1	333	
1215	31583	C	1229	1	249	
1216	31584	C	1230	1	249	
1217	31585	B	1231	147	297	
1218	31586	B	1232	1	714	
1219	31587	B	1233	1	1587	
1220	31588	C	1234	103	243	
1221	31589	C	1235	133	509	
1222	31590	B	1236	1	1594	
1223	31591	B	1237	1	628	
1224	31592	B	1238	1	948	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Met hod	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
1225	31593	B	1239	382	1020	
1226	31594	B	1240	163	5459	
1227	31595	B	1241	1	1386	
1228	31596	B	1242	44	344	
1229	31597	B	1243	6	398	
1230	31598	B	1244	77	468	
1231	31599	B	1245	520	2001	
1232	31600	B	1246	1	645	
1233	31601	B	1247	91	690	
1234	31602	B	1248	70	382	
1235	31603	B	1249	183	427	
1236	31604	B	1250	159	621	
1237	31605	B	1251	34	259	
1238	31606	B	1252	155	496	
1239	31607	B	1253	1	1416	
1240	31608	C	1254	18	355	
1241	31609	C	1255	665	826	
1242	31610	B	1256	1	559	
1243	31611	B	1257	343	1329	
1244	31612	B	1258	1	265	
1245	31613	B	1259	1	5081	
1246	31614	B	1260	373	1395	
1247	31615	B	1261	83	373	
1248	31616	B	1262	298	1252	
1249	31617	C	1263	142	327	
1250	31618	B	1264	1	237	
1251	31619	C	1265	1	330	
1252	31620	C	1266	20	358	
1253	31621	C	1267	347	493	
1254	31622	B	1268	220	1314	
1255	31623	B	1269	1	1244	
1256	31624	B	1270	35	368	
1257	31625	B	1271	145	444	
1258	31626	B	1272	1	657	
1259	31627	B	1273	84	273	
1260	31628	C	1274	47	148	
1261	31629	B	1275	1	528	
1262	31630	B	1276	34	1370	
1263	31631	C	1277	81	299	
1264	31632	C	1278	22	201	
1265	31633	B	1279	1	672	
1266	31634	B	1280	1	753	
1267	31635	C	1281	14	79	
1268	31636	C	1282	61	227	
1269	31637	B	1283	95	1124	
1270	31638	B	1284	1	891	
1271	31639	B	1285	1	1323	
1272	31640	B	1286	11	127	
1273	31641	B	1287	281	437	
1274	31642	C	1288	62	136	
1275	31643	B	1289	251	874	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
1276	31644	C	1290	16	231	
1277	31645	C	1291	299	412	
1278	31646	B	1292	310	968	
1279	31647	B	1293	237	1802	
1280	31648	B	1294	337	1143	
1281	31649	C	1295	75	176	
1282	31650	C	1296	193	414	
1283	31651	C	1297	98	679	
1284	31652	B	1298	186	260	
1285	31653	B	1299	1	732	
1286	31654	B	1300	123	268	
1287	31655	C	1301	1	420	
1288	31656	C	1302	86	223	
1289	31657	B	1303	1	594	
1290	31658	B	1304	1	4464	
1291	31659	C	1305	1	531	
1292	31660	B	1307	1	780	
1293	31661	C	1308	1	249	
1294	31662	B	1309	1	139	
1295	31663	B	1310	1	156	
1296	31664	B	1311	38	403	
1297	31665	B	1312	128	1089	
1298	31666	C	1313	262	429	
1299	31667	C	1314	209	592	
1300	31668	B	1315	1	684	
1301	31669	C	1316	1	339	
1302	31670	C	1317	71	310	
1303	31671	B	1318	1	476	
1304	31672	B	1319	133	198	
1305	31673	B	1320	1	227	
1306	31674	C	1321	612	977	
1307	31675	C	1322	65	523	
1308	31676	C	1323	35	121	
1309	31677	B	1324	8	430	
1310	31678	C	1325	1	438	
1311	31679	B	1326	1935	3296	
1312	31680	B	1332	254	462	
1313	31681	B	1333	1006	1540	
1314	31682	B	1335	127	1799	
1315	31683	B	1336	221	402	
1316	31684	C	1337	1	567	
1317	31685	C	1338	193	342	
1318	31686	B	1339	652	775	
1319	31687	B	1340	1	552	
1320	31688	B	1341	83	318	
1321	31689	B	1342	166	352	
1322	31690	C	1343	1	228	
1323	31691	B	1344	25	244	
1324	31692	C	1345	58	285	
1325	31693	B	1346	34	822	
1326	31694	B	1347	1	1563	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
1327	31695	B	1348	229	1185	
1328	31696	B	1349	59	819	
1329	31697	B	1350	1	5955	
1330	31698	B	1351	1	654	
1331	31699	B	1352	1	1299	
1332	31700	B	1353	943	1872	
1333	31701	B	1354	1	942	
1334	31702	B	1355	444	560	
1335	31703	B	1356	1	1605	
1336	31704	B	1357	1	831	
1337	31705	C	1358	48	383	
1338	31706	C	1359	1	318	
1339	31707	B	1360	186	470	
1340	31708	C	1361	1	321	
1341	31709	B	1362	1	720	
1342	31710	B	1363	1	939	
1343	31711	B	1364	1	576	
1344	31712	B	1365	1	114	
1345	31713	B	1366	129	588	
1346	31714	B	1367	24	724	
1347	31715	B	1368	1	1840	
1348	31716	B	1369	14	350	
1349	31717	B	1370	1	3187	
1350	31718	C	1371	1	261	
1351	31719	B	1372	117	890	
1352	31720	B	1373	1	438	
1353	31721	B	1374	1	217	
1354	31722	B	1375	1	160	
1355	31723	C	1376	6	191	
1356	31724	B	1377	1	759	
1357	31725	B	1378	10	251	
1358	31726	B	1379	1	719	
1359	31727	C	1380	425	886	
1360	31728	C	1381	1	216	
1361	31729	C	1382	38	229	
1362	31730	B	1383	38	672	
1363	31731	B	1384	1	1845	
1364	31732	B	1385	1	2590	
1365	31733	B	1386	32	108	
1366	31734	C	1387	215	460	
1367	31735	B	1388	1	1008	
1368	31736	B	1389	1	368	
1369	31737	B	1390	44	2402	
1370	31738	B	1391	80	1617	
1371	31739	C	1392	199	531	
1372	31740	B	1393	1	465	
1373	31741	C	1394	415	612	
1374	31742	B	1395	16	147	
1375	31743	B	1396	1	1314	
1376	31744	B	1397	1	465	
1377	31745	B	1398	1	1569	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
1378	31746	B	1399	1	490	
1379	31747	B	1400	405	573	
1380	31748	B	1401	1	2106	
1381	31749	B	1402	1	1593	
1382	31750	B	1403	1	666	
1383	31751	B	1404	1	652	
1384	31752	B	1405	352	1239	
1385	31753	B	1406	1	3184	
1386	31754	B	1407	467	1433	
1387	31755	B	1408	95	428	
1388	31756	C	1409	164	208	
1389	31757	C	1410	118	511	
1390	31758	C	1411	339	431	
1391	31759	B	1412	1	396	
1392	31760	B	1413	1	663	
1393	31761	B	1414	1	864	
1394	31762	C	1415	1	471	
1395	31763	B	1416	1	642	
1396	31764	B	1417	594	1764	
1397	31765	B	1418	1	771	
1398	31766	B	1419	1	5131	
1399	31767	B	1420	60	617	
1400	31768	B	1421	587	1202	
1401	31769	C	1422	336	638	
1402	31770	C	1423	30	200	
1403	31771	B	1424	1	1363	
1404	31772	B	1425	1	1113	
1405	31773	B	1426	1	1101	
1406	31774	B	1427	575	805	
1407	31775	C	1428	1	149	
1408	31776	C	1429	1	294	
1409	31777	C	1430	228	469	
1410	31778	B	1431	182	518	
1411	31779	B	1432	239	448	
1412	31780	B	1433	1	434	
1413	31781	C	1434	24	290	
1414	31782	C	1435	334	459	
1415	31783	B	1436	69	320	
1416	31784	B	1437	1	426	
1417	31785	B	1438	605	1423	
1418	31786	C	1439	9	113	
1419	31787	B	1440	1	58	
1420	31788	B	1441	1	210	
1421	31789	B	1442	1	2985	
1422	31790	C	1443	152	292	
1423	31791	B	1444	57	849	
1424	31792	C	1445	41	142	
1425	31793	C	1446	38	341	
1426	31794	C	1447	220	450	
1427	31795	C	1448	154	469	
1428	31796	B	1449	139	1023	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Met hod	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
1429	31797	B	1450	55	2370	
1430	31798	B	1451	1	1707	
1431	31799	B	1452	566	2356	
1432	31800	B	1453	72	255	
1433	31801	B	1454	51	182	
1434	31802	B	1455	466	600	
1435	31803	B	1456	481	1209	
1436	31804	B	1457	1	1638	
1437	31805	B	1458	8	874	
1438	31806	B	1459	1	552	
1439	31807	B	1460	1	2566	
1440	31808	B	1461	85	270	
1441	31809	B	1462	159	392	
1442	31810	B	1463	88	459	
1443	31811	B	1464	131	406	
1444	31812	B	1465	69	194	
1445	31813	B	1466	59	3134	
1446	31814	B	1467	1	3097	
1447	31815	B	1468	328	519	
1448	31816	C	1469	40	436	
1449	31817	B	1470	1	981	
1450	31818	B	1471	30	285	
1451	31819	B	1475	93	932	
1452	31820	B	1476	1	369	
1453	31821	C	1477	102	227	
1454	31822	B	1478	613	679	
1455	31823	B	1479	51	587	
1456	31824	C	1480	3	188	
1457	31825	B	1481	1	1434	
1458	31826	C	1482	27	173	
1459	31827	C	1483	294	503	
1460	31828	C	1484	506	718	
1461	31829	C	1485	97	504	
1462	31830	C	1486	27	185	
1463	31831	B	1487	50	3247	
1464	31832	B	1488	1	1032	
1465	31833	B	1489	8	95	
1466	31834	B	1490	17	303	
1467	31835	B	1491	34	81	
1468	31836	B	1492	1	1110	
1469	31837	B	1493	1	928	
1470	31838	C	1494	498	704	
1471	31839	B	1495	4	747	
1472	31840	B	1496	1	933	
1473	31841	B	1497	137	687	
1474	31842	B	1498	1524	1676	
1475	31843	B	1499	1	156	
1476	31844	B	1500	1	1126	
1477	31845	B	1501	122	765	
1478	31846	B	1503	95	304	
1479	31847	B	1504	1	156	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540.217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
1480	31848	C	1505	12	173	
1481	31849	B	1506	10	252	
1482	31850	B	1507	25	301	
1483	31851	B	1508	34	267	
1484	31852	B	1509	10	366	
1485	31853	B	1510	536	2776	
1486	31854	B	1511	1	276	
1487	31855	B	1512	1	420	
1488	31856	B	1513	235	363	
1489	31857	B	1514	664	741	
1490	31858	C	1515	312	452	
1491	31859	B	1516	1	504	
1492	31860	B	1517	52	346	
1493	31861	B	1518	458	1283	
1494	31862	B	1519	324	473	
1495	31863	B	1520	137	286	
1496	31864	B	1521	1	2682	
1497	31865	B	1522	352	1132	
1498	31866	B	1523	245	397	
1499	31867	C	1524	371	661	
1500	31868	B	1525	69	325	
1501	31869	B	1526	38	997	
1502	31870	B	1527	1	1753	
1503	31871	B	1528	215	2588	
1504	31872	C	1529	38	124	
1505	31873	C	1530	33	317	
1506	31874	C	1531	224	379	
1507	31875	B	1532	1	480	
1508	31876	C	1533	145	256	
1509	31877	C	1534	64	198	
1510	31878	B	1535	1	394	
1511	31879	C	1536	1	696	
1512	31880	B	1537	67	246	
1513	31881	C	1538	95	253	
1514	31882	B	1539	145	476	
1515	31883	C	1540	1	361	
1516	31884	C	1541	1	276	
1517	31885	B	1542	1	658	
1518	31886	B	1543	1	623	
1519	31887	C	1544	187	465	
1520	31888	C	1545	1	207	
1521	31889	C	1546	24	512	
1522	31890	C	1547	20	121	
1523	31891	B	1548	1	785	
1524	31892	B	1549	1	498	
1525	31893	C	1550	17	118	
1526	31894	C	1551	1	291	
1527	31895	B	1552	1	504	
1528	31896	B	1553	62	413	
1529	31897	B	1554	1	282	
1530	31898	C	1555	236	408	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
1531	31899	C	1556	220	398	
1532	31900	C	1557	1	732	
1533	31901	C	1558	1	372	
1534	31902	B	1559	1	1086	
1535	31903	C	1560	286	642	
1536	31904	B	1561	8	339	
1537	31905	B	1562	16	88	
1538	31906	C	1563	227	405	
1539	31907	B	1564	253	693	
1540	31908	C	1565	1	129	
1541	31909	B	1566	1	390	
1542	31910	B	1567	1	1377	
1543	31911	C	1568	16	264	
1544	31912	C	1569	51	269	
1545	31913	C	1570	39	266	
1546	31914	B	1571	200	260	
1547	31915	B	1572	220	372	
1548	31916	B	1573	1	377	
1549	31917	C	1574	280	441	
1550	31918	C	1575	50	131	
1551	31919	C	1576	47	265	
1552	31920	C	1577	10	291	
1553	31921	B	1578	1	522	
1554	31922	B	1579	756	1166	
1555	31923	B	1580	382	1228	
1556	31924	B	1581	63	229	
1557	31925	B	1582	1	452	
1558	31926	C	1583	299	556	
1559	31927	B	1584	1	870	
1560	31928	B	1585	1	708	
1561	31929	C	1586	1	420	
1562	31930	B	1587	1	1011	
1563	31931	C	1588	84	176	
1564	31932	C	1589	52	201	
1565	31933	C	1590	55	154	
1566	31934	C	1591	1	390	
1567	31935	C	1592	15	317	
1568	31936	B	1593	1	501	
1569	31937	B	1594	306	398	
1570	31938	B	1595	204	402	
1571	31939	C	1596	30	155	
1572	31940	B	1597	1	2274	
1573	31941	B	1598	1	486	
1574	31942	C	1599	148	504	
1575	31943	C	1600	82	282	
1576	31944	C	1601	82	282	
1577	31945	B	1602	66	395	
1578	31946	B	1603	114	237	
1579	31947	B	1604	1	1326	
1580	31948	B	1605	1	1900	
1581	31949	B	1606	1	1548	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Met hod	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
1582	31950	B	1607	1	1440	
1583	31951	B	1608	1	1878	
1584	31952	C	1609	402	563	
1585	31953	B	1610	1	2964	
1586	31954	B	1611	1	1284	
1587	31955	C	1612	144	449	
1588	31956	B	1613	1	1050	
1589	31957	B	1614	1	561	
1590	31958	B	1615	127	330	
1591	31959	C	1616	202	443	
1592	31960	B	1617	1	924	
1593	31961	C	1618	60	419	
1594	31962	C	1619	285	602	
1595	31963	C	1620	1	93	
1596	31964	B	1621	1	480	
1597	31965	B	1622	96	416	
1598	31966	B	1623	78	1581	
1599	31967	B	1624	1	2259	
1600	31968	C	1625	180	371	
1601	31969	B	1626	1	852	
1602	31970	B	1627	1	204	
1603	31971	B	1628	37	2613	
1604	31972	B	1629	66	1505	
1605	31973	B	1630	1	1792	
1606	31974	B	1631	100	522	
1607	31975	B	1632	252	2347	
1608	31976	C	1633	294	450	
1609	31977	C	1634	118	372	
1610	31978	B	1635	1	799	
1611	31979	B	1636	1	2496	
1612	31980	B	1637	100	1188	
1613	31981	B	1638	35	1654	
1614	31982	B	1639	46	783	
1615	31983	B	1640	8	1428	
1616	31984	B	1641	1	2121	
1617	31985	B	1642	92	667	
1618	31986	B	1643	1	339	
1619	31987	C	1644	79	434	
1620	31988	C	1645	592	921	
1621	31989	C	1646	1	171	
1622	31990	C	1647	76	264	
1623	31991	B	1648	157	912	
1624	31992	B	1649	10	462	
1625	31993	C	1650	10	333	
1626	31994	C	1651	763	1001	
1627	31995	B	1652	202	701	
1628	31996	C	1653	215	572	
1629	31997	B	1654	261	399	
1630	31998	C	1655	623	749	
1631	31999	B	1656	198	1524	
1632	32000	B	1657	108	575	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
1633	32001	B	1658	40	2173	
1634	32002	B	1659	1	479	
1635	32003	B	1660	1	1542	
1636	32004	B	1661	1	849	
1637	32005	B	1662	1	684	
1638	32006	B	1663	1	318	
1639	32007	B	1664	1	406	
1640	32008	B	1665	1	393	
1641	32009	B	1666	1	210	
1642	32010	B	1667	1	450	
1643	32011	B	1668	1	471	
1644	32012	B	1669	1	471	
1645	32013	B	1670	282	580	
1646	32014	B	1671	1	789	
1647	32015	B	1672	1	324	
1648	32016	B	1673	1	465	
1649	32017	B	1674	1	948	
1650	32018	C	1675	24	401	
1651	32019	B	1676	46	401	
1652	32020	B	1677	251	1041	
1653	32021	C	1678	1	177	
1654	32022	B	1679	1	189	
1655	32023	B	1680	65	769	
1656	32024	C	1681	1	564	
1657	32025	B	1682	65	769	
1658	32026	B	1683	1	1743	
1659	32027	B	1684	1	615	
1660	32028	B	1685	1	323	
1661	32029	B	1686	1	618	
1662	32030	B	1687	1	579	
1663	32031	C	1688	142	216	
1664	32032	C	1689	145	432	
1665	32033	B	1690	1	729	
1666	32034	C	1691	1	192	
1667	32035	C	1692	1	474	
1668	32036	B	1693	326	1662	
1669	32037	B	1694	50	1462	
1670	32038	C	1695	1	432	
1671	32039	B	1696	173	375	
1672	32040	B	1697	1	1917	
1673	32041	B	1698	57	365	
1674	32042	B	1699	78	1250	
1675	32043	B	1700	8	2210	
1676	32044	B	1701	1	474	
1677	32045	B	1702	47	879	
1678	32046	B	1703	1	465	
1679	32047	B	1704	65	473	
1680	32048	B	1705	89	1908	
1681	32049	C	1706	1	612	
1682	32050	C	1707	80	226	
1683	32051	B	1708	992	2023	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
1684	32052	B	1709	1293	1497	
1685	32053	B	1710	29	1480	
1686	32054	C	1711	1664	2179	
1687	32055	B	1712	183	8544	
1688	32056	C	1713	60	472	
1689	32057	B	1714	202	735	
1690	32058	B	1715	532	661	
1691	32059	B	1716	1	453	
1692	32060	B	1717	24	320	
1693	32061	B	1718	59	583	
1694	32062	B	1719	1	369	
1695	32063	B	1720	51	204	
1696	32064	B	1721	318	849	
1697	32065	B	1722	1	597	
1698	32066	B	1723	1	325	
1699	32067	B	1724	1	675	
1700	32068	B	1725	1	631	
1701	32069	B	1726	1	1017	
1702	32070	B	1727	158	727	
1703	32071	B	1728	296	798	
1704	32072	B	1729	1	1128	
1705	32073	C	1730	237	356	
1706	32074	C	1731	393	519	
1707	32075	B	1732	1	6432	
1708	32076	B	1733	124	402	
1709	32077	B	1734	35	421	
1710	32078	C	1735	203	385	
1711	32079	B	1736	16	406	
1712	32080	B	1737	21	306	
1713	32081	B	1738	97	352	
1714	32082	B	1739	64	7164	
1715	32083	B	1740	553	1197	
1716	32084	B	1741	553	720	
1717	32085	B	1742	1	4029	
1718	32086	B	1743	63	422	
1719	32087	B	1744	342	451	
1720	32088	B	1745	1	1238	
1721	32089	B	1746	1	2393	
1722	32090	B	1747	1667	1833	
1723	32091	C	1748	33	287	
1724	32092	B	1749	1	469	
1725	32093	B	1750	75	166	
1726	32094	B	1751	120	756	
1727	32095	C	1752	1	1098	
1728	32096	B	1753	1	486	
1729	32097	C	1754	25	374	
1730	32098	C	1755	149	394	
1731	32099	B	1756	1	660	
1732	32100	B	1757	26	391	
1733	32101	B	1758	282	419	
1734	32102	B	1759	132	717	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
1735	32103	B	1760	127	698	
1736	32104	B	1761	56	549	
1737	32105	B	1762	325	2681	
1738	32106	C	1763	465	893	
1739	32107	C	1764	123	764	
1740	32108	B	1765	206	402	
1741	32109	B	1766	393	900	
1742	32110	C	1767	1	360	
1743	32111	B	1768	285	482	
1744	32112	B	1769	1	405	
1745	32113	C	1770	304	399	
1746	32114	B	1771	1	273	
1747	32115	B	1772	67	1464	
1748	32116	B	1773	1	1122	
1749	32117	B	1774	1	1185	
1750	32118	B	1775	44	145	
1751	32119	B	1776	1	1050	
1752	32120	B	1777	250	762	
1753	32121	B	1778	1	390	
1754	32122	B	1779	172	867	
1755	32123	B	1780	327	637	
1756	32124	B	1781	1	1101	
1757	32125	C	1782	10	216	
1758	32126	B	1783	1	1449	
1759	32127	B	1784	1	402	
1760	32128	C	1785	134	418	
1761	32129	B	1786	1	417	
1762	32130	B	1787	1	384	
1763	32131	C	1788	1	738	
1764	32132	C	1789	68	280	
1765	32133	B	1790	101	327	
1766	32134	B	1791	1	1257	
1767	32135	C	1792	168	311	
1768	32136	B	1793	33	120	
1769	32137	C	1794	1	150	
1770	32138	C	1795	1	378	
1771	32139	C	1796	100	267	
1772	32140	C	1797	1	318	
1773	32141	C	1798	1	429	
1774	32142	C	1799	194	379	
1775	32143	B	1800	1	363	
1776	32144	B	1801	1	384	
1777	32145	B	1802	1	4462	
1778	32146	B	1803	235	425	
1779	32147	B	1804	8	1187	
1780	32148	B	1805	1	480	
1781	32149	B	1806	1	240	
1782	32150	B	1807	1	891	
1783	32151	C	1808	1	366	
1784	32152	B	1809	376	776	
1785	32153	B	1810	304	876	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
1786	32154	B	1811	1	939	
1787	32155	B	1812	4	744	
1788	32156	B	1813	1	717	
1789	32157	C	1814	67	366	
1790	32158	B	1815	185	847	
1791	32159	C	1816	1	315	
1792	32160	B	1817	87	297	
1793	32161	B	1818	1	1190	
1794	32162	B	1819	1	848	
1795	32163	B	1820	934	1158	
1796	32164	C	1821	1	477	
1797	32165	C	1822	6	125	
1798	32166	B	1823	335	536	
1799	32167	B	1824	157	324	
1800	32168	C	1825	176	361	
1801	32169	C	1826	1	120	
1802	32170	C	1827	25	360	
1803	32171	C	1828	246	377	
1804	32172	C	1829	4782	5015	
1805	32173	B	1830	1105	3034	
1806	32174	B	1831	818	874	
1807	32175	C	1832	1	444	
1808	32176	B	1833	589	734	
1809	32177	B	1834	1	264	
1810	32178	B	1835	46	112	
1811	32179	B	1836	1	360	
1812	32180	B	1837	589	734	
1813	32181	B	1838	1	675	
1814	32182	B	1839	1	1194	
1815	32183	B	1840	121	880	
1816	32184	B	1841	35	853	
1817	32185	B	1842	1	426	
1818	32186	C	1843	1	252	
1819	32187	B	1844	1	323	
1820	32188	B	1845	1	789	
1821	32189	C	1846	337	1521	
1822	32190	C	1847	1	345	
1823	32191	B	1848	331	3385	
1824	32192	B	1849	1	1584	
1825	32193	B	1850	1	957	
1826	32194	B	1851	226	1794	
1827	32195	B	1852	52	594	
1828	32196	C	1853	1	615	
1829	32197	B	1854	1	318	
1830	32198	B	1855	297	450	
1831	32199	C	1856	87	404	
1832	32200	C	1857	1	171	
1833	32201	C	1858	1	171	
1834	32202	B	1859	34	831	
1835	32203	B	1860	1	1375	
1836	32204	B	1861	1	546	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
1837	32205	C	1862	36	182	
1838	32206	B	1863	392	1043	
1839	32207	B	1864	1	1283	
1840	32208	C	1865	283	591	
1841	32209	C	1866	97	108	
1842	32210	C	1867	25	250	
1843	32211	C	1868	142	448	
1844	32212	C	1869	1	576	
1845	32213	C	1870	1	396	
1846	32214	B	1871	1	885	
1847	32215	C	1872	321	848	
1848	32216	B	1873	82	871	
1849	32217	C	1874	1	723	
1850	32218	C	1875	1	426	
1851	32219	C	1876	624	803	
1852	32220	B	1877	1	588	
1853	32221	B	1878	39	58	
1854	32222	B	1879	1	1011	
1855	32223	B	1880	1	654	
1856	32224	C	1881	1	498	
1857	32225	C	1882	1	249	
1858	32226	C	1883	507	785	
1859	32227	C	1885	310	404	
1860	32228	B	1886	448	618	
1861	32229	B	1887	1	388	
1862	32230	B	1888	106	414	
1863	32231	B	1889	82	4206	
1864	32232	B	1890	1	240	
1865	32233	B	1891	1	324	
1866	32234	C	1892	243	447	
1867	32235	C	1893	139	228	
1868	32236	C	1894	61	300	
1869	32237	C	1895	271	429	
1870	32238	B	1896	545	1054	
1871	32239	B	1897	609	706	
1872	32240	B	1898	1	2521	
1873	32241	C	1899	152	517	
1874	32242	B	1900	217	313	
1875	32243	C	1901	86	193	
1876	32244	C	1902	29	271	
1877	32245	B	1903	1	522	
1878	32246	C	1904	37	225	
1879	32247	C	1905	84	308	
1880	32248	B	1906	36	1569	
1881	32249	B	1907	1	522	
1882	32250	C	1908	1	510	
1883	32251	B	1909	1	936	
1884	32252	C	1910	1	162	
1885	32253	C	1911	155	427	
1886	32254	B	1912	1	1282	
1887	32255	B	1913	165	270	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Met hod	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
1888	32256	B	1914	513	9470	
1889	32257	B	1915	35	871	
1890	32258	B	1916	1	690	
1891	32259	C	1917	86	271	
1892	32260	B	1918	1	690	
1893	32261	C	1919	14	301	
1894	32262	B	1920	1	936	
1895	32263	B	1921	1	1901	
1896	32264	B	1922	36	238	
1897	32265	B	1923	1	738	
1898	32266	C	1924	5	364	
1899	32267	C	1925	43	494	
1900	32268	C	1926	96	263	
1901	32269	B	1927	1	207	
1902	32270	B	1928	1	290	
1903	32271	B	1929	52	482	
1904	32272	B	1930	271	408	
1905	32273	B	1931	114	309	
1906	32274	C	1932	218	398	
1907	32275	B	1933	1	1011	
1908	32276	B	1934	1	702	
1909	32277	B	1935	1	1305	
1910	32278	C	1936	141	374	
1911	32279	B	1937	1	834	
1912	32280	B	1938	47	363	
1913	32281	B	1939	73	558	
1914	32282	B	1940	373	864	
1915	32283	B	1941	96	377	
1916	32284	B	1942	55	2711	
1917	32285	B	1945	833	1352	
1918	32286	B	1946	1	1101	
1919	32287	B	1947	865	1070	
1920	32288	C	1948	1	285	
1921	32289	B	1949	1	642	
1922	32290	B	1950	124	813	
1923	32291	B	1951	1	654	
1924	32292	B	1952	180	303	
1925	32293	C	1953	15	170	
1926	32294	B	1954	245	646	
1927	32295	B	1955	100	824	
1928	32296	C	1956	52	348	
1929	32297	B	1957	1	678	
1930	32298	B	1958	1	954	
1931	32299	B	1959	1	675	
1932	32300	C	1960	52	348	
1933	32301	B	1961	71	251	
1934	32302	B	1962	427	747	
1935	32303	B	1963	1	453	
1936	32304	B	1964	1	375	
1937	32305	B	1965	117	1109	
1938	32306	C	1966	47	133	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
1939	32307	B	1967	79	1149	
1940	32308	B	1968	1	693	
1941	32309	B	1969	1	1179	
1942	32310	B	1970	1	639	
1943	32311	B	1971	502	1294	
1944	32312	C	1972	670	1185	
1945	32313	B	1973	1	1044	
1946	32314	B	1974	1	3645	
1947	32315	B	1975	1	2877	
1948	32316	B	1976	1	1579	
1949	32317	B	1977	1	750	
1950	32318	B	1978	1	438	
1951	32319	C	1979	122	307	
1952	32320	C	1980	71	271	
1953	32321	C	1981	151	363	
1954	32322	C	1982	122	307	
1955	32323	C	1983	55	282	
1956	32324	C	1984	89	385	
1957	32325	C	1985	48	275	
1958	32326	C	1986	246	557	
1959	32327	B	1987	394	2565	
1960	32328	B	1988	1	432	
1961	32329	B	1989	46	483	
1962	32330	B	1990	150	482	
1963	32331	B	1991	10	265	
1964	32332	C	1992	40	162	
1965	32333	B	1993	1	3639	
1966	32334	B	1994	83	179	
1967	32335	B	1995	39	1452	
1968	32336	B	1996	50	384	
1969	32337	B	1997	256	351	
1970	32338	B	1998	1	771	
1971	32339	B	1999	1	489	
1972	32340	B	2000	37	447	
1973	32341	B	2001	1	1272	
1974	32342	B	2002	1	2559	
1975	32343	C	2003	221	589	
1976	32344	C	2004	415	1033	
1977	32345	B	2007	318	694	
1978	32346	B	2008	31	819	
1979	32347	B	2009	1	276	
1980	32348	B	2010	1	369	
1981	32349	B	2011	85	628	
1982	32350	B	2012	19	178	
1983	32351	B	2013	217	393	
1984	32352	B	2014	1	779	
1985	32353	B	2015	107	650	
1986	32354	B	2016	313	527	
1987	32355	B	2017	32	258	
1988	32356	C	2018	51	345	
1989	32357	B	2019	1	393	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Met hod	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
1990	32358	B	2020	647	1362	
1991	32359	C	2021	16	378	
1992	32360	B	2022	32	349	
1993	32361	C	2023	256	425	
1994	32362	C	2024	134	382	
1995	32363	B	2025	138	171	
1996	32364	B	2026	1	1626	
1997	32365	B	2027	509	810	
1998	32366	C	2028	1	513	
1999	32367	C	2029	7	375	
2000	32368	C	2030	1	410	
2001	32369	B	2031	1	864	
2002	32370	B	2032	110	928	
2003	32371	B	2033	1	1026	
2004	32372	B	2034	1	1008	
2005	32373	B	2035	1	588	
2006	32374	B	2036	1	412	
2007	32375	B	2037	1	1851	
2008	32376	B	2038	309	663	
2009	32377	B	2039	1	525	
2010	32378	B	2040	1	2214	
2011	32379	B	2041	1	486	
2012	32380	B	2042	1	774	
2013	32381	B	2043	1	596	
2014	32382	B	2044	305	395	
2015	32383	C	2045	27	185	
2016	32384	B	2046	1	1071	
2017	32385	B	2047	1	1326	
2018	32386	B	2048	1	3761	
2019	32387	C	2049	55	189	
2020	32388	B	2050	1016	1683	
2021	32389	C	2051	942	1130	
2022	32390	B	2052	1	598	
2023	32391	B	2053	1	768	
2024	32392	B	2054	1	999	
2025	32393	C	2055	1	252	
2026	32394	B	2056	154	606	
2027	32395	B	2057	1	846	
2028	32396	C	2058	334	690	
2029	32397	B	2059	268	5712	
2030	32398	C	2060	117	662	
2031	32399	B	2061	1	3504	
2032	32400	B	2062	816	927	
2033	32401	B	2063	1	342	
2034	32402	B	2064	1	1443	
2035	32403	C	2065	53	102	
2036	32404	C	2066	271	528	
2037	32405	B	2067	1	843	
2038	32406	C	2068	187	408	
2039	32407	C	2069	174	320	
2040	32408	B	2070	31	534	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
2041	32409	C	2071	183	329	
2042	32410	B	2072	3	389	
2043	32411	B	2073	78	974	
2044	32412	B	2074	467	692	
2045	32413	C	2075	605	965	
2046	32414	B	2076	1	555	
2047	32415	B	2077	1	390	
2048	32416	B	2078	1	2522	
2049	32417	B	2079	24	94	
2050	32418	B	2080	78	593	
2051	32419	B	2081	1	612	
2052	32420	B	2082	42	342	
2053	32421	B	2083	1	477	
2054	32422	B	2084	57	1640	
2055	32423	C	2085	110	307	
2056	32424	B	2086	1	591	
2057	32425	C	2087	14	355	
2058	32426	B	2088	47	998	
2059	32427	B	2089	1	498	
2060	32428	C	2090	357	560	
2061	32429	B	2091	1	522	
2062	32430	C	2092	231	659	
2063	32431	C	2093	36	167	
2064	32432	B	2094	394	2695	
2065	32433	B	2096	61	2215	
2066	32434	B	2097	204	572	
2067	32435	C	2098	476	652	
2068	32436	B	2099	1	190	
2069	32437	C	2100	1	259	
2070	32438	B	2101	1	2625	
2071	32439	B	2102	1403	2950	
2072	32440	B	2103	672	1955	
2073	32441	C	2104	1	351	
2074	32442	B	2105	1	567	
2075	32443	C	2106	176	304	
2076	32444	C	2107	27	308	
2077	32445	C	2108	68	307	
2078	32446	C	2109	322	567	
2079	32447	B	2110	1	1297	
2080	32448	B	2111	281	1488	
2081	32449	B	2112	12	2497	
2082	32450	C	2113	90	284	
2083	32451	B	2114	1	2466	
2084	32452	B	2115	1	603	
2085	32453	B	2116	1	954	
2086	32454	B	2117	205	441	
2087	32455	B	2118	68	2052	
2088	32456	B	2119	271	639	
2089	32457	B	2120	1	1356	
2090	32458	B	2121	247	1326	
2091	32459	B	2122	1	1041	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Met hod	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
2092	32460	B	2123	1	1695	
2093	32461	B	2124	1	1767	
2094	32462	B	2125	1	2286	
2095	32463	B	2126	1	1167	
2096	32464	B	2127	1	2343	
2097	32465	B	2128	1	1056	
2098	32466	B	2129	1	1379	
2099	32467	B	2130	1	1839	
2100	32468	B	2131	1	5460	
2101	32469	B	2132	133	549	
2102	32470	B	2133	1	534	
2103	32471	B	2134	1	537	
2104	32472	B	2135	1	49	
2105	32473	C	2136	1	432	
2106	32474	B	2137	1	615	
2107	32475	B	2138	146	556	
2108	32476	B	2139	133	1434	
2109	32477	B	2140	1	357	
2110	32478	C	2141	1	429	
2111	32479	B	2142	1	411	
2112	32480	B	2143	1	459	
2113	32481	C	2144	224	550	
2114	32482	B	2145	1	1035	
2115	32483	B	2146	1	342	
2116	32484	C	2147	1	321	
2117	32485	C	2148	1	317	
2118	32486	B	2149	1	495	
2119	32487	B	2150	146	556	
2120	32488	C	2151	1	390	
2121	32489	C	2152	461	643	
2122	32490	C	2153	198	416	
2123	32491	C	2154	258	500	
2124	32492	B	2155	291	1034	
2125	32493	B	2156	1	834	
2126	32494	B	2157	1	7852	
2127	32495	B	2158	1	1320	
2128	32496	B	2159	1631	1756	
2129	32497	B	2160	500	8643	
2130	32498	C	2161	193	475	
2131	32499	B	2162	1	795	
2132	32500	B	2163	1	663	
2133	32501	C	2164	1	303	
2134	32502	B	2165	266	385	
2135	32503	B	2166	1	704	
2136	32504	B	2167	1	720	
2137	32505	B	2168	364	507	
2138	32506	B	2169	44	197	
2139	32507	C	2170	72	224	
2140	32508	C	2171	228	393	
2141	32509	C	2172	241	396	
2142	32510	C	2173	415	552	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
2143	32511	B	2174	64	268	
2144	32512	C	2175	1	462	
2145	32513	C	2176	1	357	
2146	32514	B	2177	1	3213	
2147	32515	B	2178	119	682	
2148	32516	B	2179	1	405	
2149	32517	B	2180	297	769	
2150	32518	B	2181	1	1314	
2151	32519	C	2182	156	287	
2152	32520	B	2183	1	756	
2153	32521	B	2184	1	645	
2154	32522	B	2185	1	948	
2155	32523	B	2186	1	660	
2156	32524	B	2187	186	518	
2157	32525	B	2188	1	3570	
2158	32526	B	2189	1	3354	
2159	32527	B	2190	1	2232	
2160	32528	B	2191	1	1356	
2161	32529	B	2192	1	1103	
2162	32530	B	2193	1	1902	
2163	32531	B	2194	1	2232	
2164	32532	B	2195	1	2991	
2165	32533	B	2196	1	2136	
2166	32534	B	2197	1	1524	
2167	32535	B	2198	1	2106	
2168	32536	B	2199	1	1224	
2169	32537	B	2200	1	1935	
2170	32538	B	2201	1	1428	
2171	32539	B	2202	1	858	
2172	32540	B	2203	1	2162	
2173	32541	B	2204	1	1374	
2174	32542	B	2205	205	3666	
2175	32543	B	2206	59	4311	
2176	32544	B	2207	1	1311	
2177	32545	B	2208	1	2742	
2178	32546	B	2209	1	1878	
2179	32547	B	2210	1	1074	
2180	32548	B	2211	1	2217	
2181	32549	B	2212	1	1945	
2182	32550	B	2213	1	1941	
2183	32551	B	2214	1	1737	
2184	32552	B	2215	1	1422	
2185	32553	B	2216	22	9087	
2186	32554	B	2217	1	4954	
2187	32555	B	2218	1	1812	
2188	32556	B	2219	1	939	
2189	32557	B	2220	1	2895	
2190	32558	B	2221	1	6223	
2191	32559	B	2222	109	4966	
2192	32560	B	2223	3807	9479	
2193	32561	B	2224	1	4903	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Met hod	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
2194	32562	B	2225	210	516	
2195	32563	C	2226	185	292	
2196	32564	B	2227	1	657	
2197	32565	B	2228	1	1011	
2198	32566	B	2229	1	1303	
2199	32567	C	2230	69	182	
2200	32568	B	2231	1	321	
2201	32569	B	2232	88	522	
2202	32570	B	2233	527	1207	
2203	32571	B	2234	118	375	
2204	32572	B	2235	8	148	
2205	32573	B	2236	609	1121	
2206	32574	B	2237	1	1500	
2207	32575	C	2238	121	330	
2208	32576	B	2239	1	591	
2209	32577	B	2240	125	471	
2210	32578	B	2241	64	909	
2211	32579	B	2242	13	579	
2212	32580	B	2243	249	531	
2213	32581	C	2244	107	928	
2214	32582	B	2245	213	322	
2215	32583	C	2246	373	441	
2216	32584	B	2247	54	2723	
2217	32585	B	2248	94	529	
2218	32586	B	2249	57	260	
2219	32587	B	2250	674	1972	
2220	32588	B	2251	1	1053	
2221	32589	C	2252	186	347	
2222	32590	B	2253	26	193	
2223	32591	B	2254	1	5442	
2224	32592	B	2255	428	3792	
2225	32593	B	2256	9	199	
2226	32594	B	2257	421	2932	
2227	32595	B	2258	305	547	
2228	32596	B	2259	1	891	
2229	32597	B	2260	1	641	
2230	32598	B	2261	108	542	
2231	32599	B	2262	105	440	
2232	32600	B	2263	553	729	
2233	32601	B	2264	1	645	
2234	32602	B	2265	291	452	
2235	32603	B	2266	143	348	
2236	32604	C	2267	310	426	
2237	32605	B	2268	1	1344	
2238	32606	B	2269	237	2834	
2239	32607	B	2270	1	2922	
2240	32608	B	2271	109	3499	
2241	32609	B	2272	1	1611	
2242	32610	B	2273	1	1575	
2243	32611	B	2274	1	1314	
2244	32612	B	2275	1	1209	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
2245	32613	B	2276	1	2022	
2246	32614	B	2277	1	1938	
2247	32615	B	2279	1	1806	
2248	32616	B	2280	1	2361	
2249	32617	B	2281	1	2732	
2250	32618	B	2282	1	3703	
2251	32619	C	2283	1	507	
2252	32620	B	2284	118	316	
2253	32621	B	2285	1	272	
2254	32622	B	2286	37	388	
2255	32623	B	2287	1	660	
2256	32624	B	2288	431	633	
2257	32625	B	2289	1	1032	
2258	32626	B	2290	1	1227	
2259	32627	C	2291	27	296	
2260	32628	B	2292	58	370	
2261	32629	B	2293	1	1275	
2262	32630	B	2294	1	1299	
2263	32631	C	2295	227	613	
2264	32632	B	2296	1	297	
2265	32633	B	2297	126	206	
2266	32634	C	2298	1	387	
2267	32635	B	2299	19	279	
2268	32636	B	2300	1	612	
2269	32637	C	2301	81	191	
2270	32638	B	2302	120	308	
2271	32639	B	2303	1	2145	
2272	32640	C	2304	270	416	
2273	32641	B	2305	31	627	
2274	32642	B	2306	128	499	
2275	32643	B	2307	61	388	
2276	32644	B	2308	744	2094	
2277	32645	B	2309	241	669	
2278	32646	B	2310	1	285	
2279	32647	B	2311	137	307	
2280	32648	C	2312	168	362	
2281	32649	C	2313	8	394	
2282	32650	B	2314	1	489	
2283	32651	C	2315	1	204	
2284	32652	B	2316	1	2361	
2285	32653	B	2317	1	2265	
2286	32654	B	2318	1	2268	
2287	32655	B	2319	1	2337	
2288	32656	B	2320	1	2196	
2289	32657	B	2321	1	2298	
2290	32658	B	2322	1	2880	
2291	32659	B	2323	1	2562	
2292	32660	B	2324	1	2835	
2293	32661	B	2325	1	2172	
2294	32662	B	2326	675	2515	
2295	32663	B	2327	1	2709	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
2296	32664	B	2328	1	2478	
2297	32665	B	2329	1	2748	
2298	32666	B	2330	877	4763	
2299	32667	B	2331	1	2590	
2300	32668	B	2332	1	597	
2301	32669	C	2333	279	412	
2302	32670	C	2334	507	878	
2303	32671	C	2335	1	147	
2304	32672	B	2336	52	573	
2305	32673	C	2337	211	446	
2306	32674	B	2338	1	1669	
2307	32675	B	2339	69	418	
2308	32676	B	2340	1	2778	
2309	32677	B	2341	1	1896	
2310	32678	B	2342	1	1836	
2311	32679	B	2343	1	2463	
2312	32680	B	2344	287	1785	
2313	32681	B	2345	1	2860	
2314	32682	B	2346	1	1281	
2315	32683	B	2347	1	1176	
2316	32684	B	2348	1	1431	
2317	32685	B	2349	1	2361	
2318	32686	B	2350	592	1815	
2319	32687	B	2351	1	2764	
2320	32688	C	2352	309	581	
2321	32689	B	2353	99	5619	
2322	32690	B	2354	133	3213	
2323	32691	B	2355	1	3193	
2324	32692	B	2356	1	3291	
2325	32693	B	2357	1	4019	
2326	32694	B	2358	167	4093	
2327	32695	B	2359	1	3534	
2328	32696	B	2360	1	3405	
2329	32697	B	2361	1	3555	
2330	32698	B	2362	1	3786	
2331	32699	B	2363	1	3414	
2332	32700	B	2364	1	5130	
2333	32701	B	2365	1	8244	
2334	32702	B	2366	1	7995	
2335	32703	B	2367	1	1980	
2336	32704	B	2368	1	4269	
2337	32705	B	2369	1	169	
2338	32706	B	2370	1	573	
2339	32707	B	2371	388	1101	
2340	32708	C	2372	1	354	
2341	32709	B	2373	134	1057	
2342	32710	B	2374	91	1464	
2343	32711	B	2375	117	767	
2344	32712	B	2376	1	486	
2345	32713	C	2377	1	726	
2346	32714	C	2378	31	447	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
2347	32715	B	2379	1	402	
2348	32716	B	2380	22	427	
2349	32717	B	2381	351	560	
2350	32718	B	2382	1	1122	
2351	32719	B	2383	1	1035	
2352	32720	B	2384	1	309	
2353	32721	B	2385	80	673	
2354	32722	B	2386	160	659	
2355	32723	B	2387	1	858	
2356	32724	C	2388	228	365	
2357	32725	B	2389	1	531	
2358	32726	B	2390	218	670	
2359	32727	C	2391	182	484	
2360	32728	C	2392	1	738	
2361	32729	C	2393	27	316	
2362	32730	B	2394	291	498	
2363	32731	C	2395	230	409	
2364	32732	B	2396	228	1361	
2365	32733	C	2397	210	548	
2366	32734	B	2398	309	1202	
2367	32735	C	2399	100	406	
2368	32736	B	2400	440	2579	
2369	32737	C	2401	102	359	
2370	32738	B	2402	1	414	
2371	32739	B	2403	717	976	
2372	32740	B	2404	1	777	
2373	32741	B	2405	1	208	
2374	32742	B	2406	1	570	
2375	32743	B	2407	187	525	
2376	32744	B	2408	20	499	
2377	32745	B	2409	1	210	
2378	32746	B	2410	41	166	
2379	32747	B	2411	29	348	
2380	32748	B	2412	1	564	
2381	32749	C	2413	250	366	
2382	32750	B	2414	164	430	
2383	32751	C	2415	141	340	
2384	32752	B	2416	304	422	
2385	32753	B	2417	1	2031	
2386	32754	B	2418	1	1527	
2387	32755	B	2419	1	2892	
2388	32756	B	2420	218	4186	
2389	32757	B	2421	203	655	
2390	32758	C	2422	1	346	
2391	32759	B	2423	299	433	
2392	32760	B	2424	172	525	
2393	32761	B	2425	1	3270	
2394	32762	B	2426	202	481	
2395	32763	B	2427	148	3473	
2396	32764	C	2428	182	460	
2397	32765	B	2429	116	2953	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Met hod	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
2398	32766	B	2430	153	332	
2399	32767	B	2431	267	2752	
2400	32768	B	2432	1	848	
2401	32769	C	2433	54	350	
2402	32770	B	2434	160	531	
2403	32771	B	2435	159	184	
2404	32772	B	2436	44	293	
2405	32773	C	2437	129	438	
2406	32774	C	2438	255	469	
2407	32775	B	2439	292	456	
2408	32776	B	2440	86	225	
2409	32777	B	2441	1	603	
2410	32778	B	2442	305	402	
2411	32779	C	2443	117	332	
2412	32780	B	2444	1	642	
2413	32781	B	2445	50	238	
2414	32782	B	2446	350	1331	
2415	32783	B	2447	1	867	
2416	32784	B	2448	1	498	
2417	32785	B	2449	40	849	
2418	32786	B	2450	187	404	
2419	32787	B	2451	1	921	
2420	32788	B	2452	439	517	
2421	32789	C	2453	143	682	
2422	32790	B	2454	87	401	
2423	32791	B	2455	44	277	
2424	32792	B	2456	1	639	
2425	32793	B	2457	1	816	
2426	32794	B	2458	100	454	
2427	32795	C	2459	717	923	
2428	32796	C	2460	1	412	
2429	32797	C	2461	80	394	
2430	32798	B	2462	278	323	
2431	32799	C	2463	9	239	
2432	32800	B	2464	1	537	
2433	32801	B	2465	1	798	
2434	32802	B	2466	1	861	
2435	32803	B	2467	611	979	
2436	32804	B	2468	56	166	
2437	32805	C	2469	40	495	
2438	32806	B	2470	1	216	
2439	32807	B	2471	273	385	
2440	32808	B	2472	77	489	
2441	32809	C	2473	480	791	
2442	32810	B	2474	110	1318	
2443	32811	B	2475	114	563	
2444	32812	B	2476	813	3193	
2445	32813	C	2477	198	650	
2446	32814	B	2478	1	234	
2447	32815	B	2479	7	174	
2448	32816	B	2480	1	1035	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
2449	32817	B	2481	1	564	
2450	32818	B	2482	16	894	
2451	32819	B	2483	1	207	
2452	32820	B	2484	1	2742	
2453	32821	B	2485	1	1071	
2454	32822	B	2486	58	1228	
2455	32823	C	2487	51	179	
2456	32824	B	2488	1	1119	
2457	32825	C	2489	147	398	
2458	32826	C	2490	1	504	
2459	32827	C	2491	4	240	
2460	32828	B	2492	190	388	
2461	32829	B	2493	1	594	
2462	32830	C	2494	299	477	
2463	32831	B	2495	1	2328	
2464	32832	C	2496	1	924	
2465	32833	B	2497	1	2703	
2466	32834	B	2498	504	1392	
2467	32835	C	2499	649	1239	
2468	32836	B	2500	46	842	
2469	32837	B	2501	251	555	
2470	32838	B	2502	258	326	
2471	32839	B	2503	49	386	
2472	32840	C	2504	63	383	
2473	32841	B	2505	150	585	
2474	32842	B	2506	65	678	
2475	32843	C	2507	477	634	
2476	32844	B	2508	80	337	
2477	32845	B	2509	1	1233	
2478	32846	B	2510	1	2526	
2479	32847	B	2511	192	2617	
2480	32848	B	2512	1	921	
2481	32849	B	2513	1	1650	
2482	32850	B	2514	79	1587	
2483	32851	B	2515	1	657	
2484	32852	B	2516	1	1260	
2485	32853	B	2517	1	762	
2486	32854	C	2518	1	729	
2487	32855	B	2519	1	1299	
2488	32856	B	2520	1	882	
2489	32857	C	2521	1	369	
2490	32858	B	2522	52	573	
2491	32859	B	2523	1	570	
2492	32860	B	2524	1	2376	
2493	32861	B	2525	1	786	
2494	32862	B	2526	1	760	
2495	32863	B	2527	73	714	
2496	32864	B	2528	1	2976	
2497	32865	B	2529	1	1021	
2498	32866	B	2530	1	1386	
2499	32867	B	2531	352	1239	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Met hod	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
2500	32868	B	2532	1	1740	
2501	32869	B	2533	1	915	
2502	32870	B	2534	392	1393	
2503	32871	B	2535	1	4868	
2504	32872	B	2536	1	2667	
2505	32873	B	2537	1	825	
2506	32874	B	2538	1	735	
2507	32875	B	2539	88	469	
2508	32876	C	2540	1	390	
2509	32877	C	2541	113	328	
2510	32878	B	2542	475	848	
2511	32879	B	2543	472	1482	
2512	32880	C	2544	42	593	
2513	32881	B	2545	470	998	
2514	32882	B	2546	83	339	
2515	32883	B	2547	1	501	
2516	32884	B	2548	1198	1432	
2517	32885	B	2549	1	486	
2518	32886	B	2550	454	1626	
2519	32887	C	2551	227	388	
2520	32888	B	2552	25	687	
2521	32889	B	2553	569	753	
2522	32890	C	2554	147	384	
2523	32891	B	2555	210	419	
2524	32892	B	2556	1	1185	
2525	32893	C	2557	93	257	
2526	32894	C	2558	41	375	
2527	32895	C	2559	155	579	
2528	32896	B	2560	1	375	
2529	32897	C	2561	37	351	
2530	32898	C	2562	39	518	
2531	32899	B	2563	310	493	
2532	32900	C	2564	83	373	
2533	32901	B	2565	120	843	
2534	32902	C	2566	327	468	
2535	32903	B	2567	1	732	
2536	32904	C	2568	243	434	
2537	32905	C	2569	117	347	
2538	32906	C	2570	1	363	
2539	32907	C	2571	1	219	
2540	32908	B	2572	82	390	
2541	32909	B	2573	1152	1737	
2542	32910	C	2574	294	524	
2543	32911	B	2575	1	345	
2544	32912	B	2576	106	1073	
2545	32913	B	2577	1	313	
2546	32914	C	2578	1	594	
2547	32915	C	2579	16	102	
2548	32916	C	2580	1	441	
2549	32917	B	2581	1	462	
2550	32918	B	2582	113	1257	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
2551	32919	B	2583	1	402	
2552	32920	B	2584	489	570	
2553	32921	B	2585	218	356	
2554	32922	C	2586	225	345	
2555	32923	C	2587	472	621	
2556	32924	B	2588	1	984	
2557	32925	B	2589	1	1119	
2558	32926	B	2590	1	771	
2559	32927	B	2591	97	681	
2560	32928	B	2592	112	202	
2561	32929	C	2593	1	381	
2562	32930	C	2594	115	321	
2563	32931	C	2595	3	200	
2564	32932	B	2596	212	303	
2565	32933	C	2597	236	396	
2566	32934	B	2598	119	625	
2567	32935	C	2599	68	334	
2568	32936	C	2600	85	351	
2569	32937	B	2601	1	723	
2570	32938	C	2602	235	463	
2571	32939	B	2603	1	498	
2572	32940	C	2604	179	346	
2573	32941	B	2605	21	486	
2574	32942	B	2606	20	600	
2575	32943	B	2607	172	294	
2576	32944	B	2608	130	1200	
2577	32945	B	2609	61	243	
2578	32946	B	2610	1	753	
2579	32947	B	2611	1	2274	
2580	32948	B	2612	1	1848	
2581	32949	B	2613	1	1263	
2582	32950	B	2614	412	654	
2583	32951	C	2615	176	658	
2584	32952	B	2616	310	628	
2585	32953	B	2617	1	579	
2586	32954	C	2618	145	309	
2587	32955	B	2619	298	353	
2588	32956	B	2620	163	594	
2589	32957	B	2621	1	468	
2590	32958	B	2622	1	552	
2591	32959	B	2623	1	876	
2592	32960	B	2624	140	1333	
2593	32961	C	2625	1	222	
2594	32962	B	2626	1	645	
2595	32963	C	2627	49	339	
2596	32964	B	2628	1	1944	
2597	32965	C	2629	79	189	
2598	32966	C	2630	513	767	
2599	32967	B	2631	114	230	
2600	32968	B	2632	24	629	
2601	32969	B	2633	98	230	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
2602	32970	B	2634	99	462	
2603	32971	B	2635	127	1498	
2604	32972	B	2636	22	105	
2605	32973	B	2637	1	1173	
2606	32974	B	2638	403	660	
2607	32975	B	2639	58	507	
2608	32976	C	2640	103	480	
2609	32977	B	2641	1	657	
2610	32978	B	2642	1	508	
2611	32979	B	2643	1	999	
2612	32980	C	2644	1	756	
2613	32981	C	2645	1	675	
2614	32982	B	2646	1	810	
2615	32983	B	2647	1	334	
2616	32984	B	2648	1	781	
2617	32985	B	2649	76	211	
2618	32986	B	2650	1	687	
2619	32987	B	2651	1	753	
2620	32988	B	2652	37	1038	
2621	32989	B	2653	1	456	
2622	32990	B	2654	1	168	
2623	32991	B	2655	1	786	
2624	32992	C	2656	571	1278	
2625	32993	C	2657	96	548	
2626	32994	C	2658	391	504	
2627	32995	B	2659	1	183	
2628	32996	C	2660	1	381	
2629	32997	B	2661	1	642	
2630	32998	B	2662	1	1164	
2631	32999	B	2663	1	471	
2632	33000	B	2664	1	972	
2633	33001	C	2665	75	182	
2634	33002	C	2666	125	226	
2635	33003	B	2667	1	462	
2636	33004	B	2668	1	422	
2637	33005	B	2669	81	616	
2638	33006	B	2670	197	713	
2639	33007	B	2671	1	882	
2640	33008	B	2672	1	507	
2641	33009	C	2673	176	274	
2642	33010	B	2674	250	446	
2643	33011	B	2675	19	118	
2644	33012	B	2676	21	120	
2645	33013	B	2677	373	389	
2646	33014	B	2678	1	1452	
2647	33015	B	2679	70	148	
2648	33016	C	2680	7	96	
2649	33017	C	2681	360	550	
2650	33018	B	2682	55	1618	
2651	33019	B	2683	1	309	
2652	33020	B	2684	100	528	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
2653	33021	B	2685	1	1191	
2654	33022	B	2686	52	834	
2655	33023	B	2687	1	933	
2656	33024	C	2688	80	322	
2657	33025	B	2689	127	415	
2658	33026	B	2690	74	190	
2659	33027	B	2691	150	380	
2660	33028	B	2692	1	1098	
2661	33029	C	2693	185	502	
2662	33030	B	2694	1	180	
2663	33031	C	2695	257	498	
2664	33032	B	2696	88	409	
2665	33033	C	2697	720	902	
2666	33034	C	2698	201	437	
2667	33035	C	2699	16	189	
2668	33036	B	2701	1	2286	
2669	33037	B	2702	1	1026	
2670	33038	B	2703	777	1035	
2671	33039	B	2704	1	1200	
2672	33040	B	2705	332	462	
2673	33041	B	2706	351	480	
2674	33042	B	2707	10	327	
2675	33043	B	2708	108	1325	
2676	33044	B	2709	36	189	
2677	33045	B	2710	54	3192	
2678	33046	B	2711	1	3423	
2679	33047	C	2712	5	280	
2680	33048	C	2713	1	88	
2681	33049	C	2714	1	153	
2682	33050	B	2715	70	231	
2683	33051	B	2716	11	427	
2684	33052	B	2717	74	943	
2685	33053	C	2718	109	315	
2686	33054	B	2719	1	335	
2687	33055	B	2720	108	506	
2688	33056	C	2721	1	486	
2689	33057	C	2722	87	441	
2690	33058	C	2723	85	276	
2691	33059	C	2724	86	280	
2692	33060	C	2725	108	254	
2693	33061	B	2726	1	930	
2694	33062	B	2727	23	847	
2695	33063	B	2728	19	182	
2696	33064	C	2729	190	300	
2697	33065	B	2730	67	650	
2698	33066	B	2731	1	1149	
2699	33067	B	2732	1	263	
2700	33068	B	2733	73	676	
2701	33069	B	2734	1	414	
2702	33070	B	2735	4	256	
2703	33071	B	2736	29	493	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540.217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
2704	33072	B	2737	1	1323	
2705	33073	B	2738	1	4209	
2706	33074	B	2739	538	728	
2707	33075	B	2740	344	1447	
2708	33076	C	2741	223	477	
2709	33077	B	2742	1	1091	
2710	33078	B	2743	1	2865	
2711	33079	B	2744	1	1203	
2712	33080	C	2745	120	401	
2713	33081	B	2746	1	688	
2714	33082	B	2747	1	549	
2715	33083	B	2748	196	1647	
2716	33084	B	2749	1	378	
2717	33085	C	2750	2	166	
2718	33086	B	2751	1	807	
2719	33087	C	2752	343	532	
2720	33088	B	2753	1	885	
2721	33089	C	2754	32	247	
2722	33090	B	2755	1	1152	
2723	33091	B	2756	1	885	
2724	33092	B	2757	87	359	
2725	33093	B	2758	71	418	
2726	33094	B	2759	117	1983	
2727	33095	B	2760	176	1045	
2728	33096	B	2761	25	187	
2729	33097	B	2762	1	315	
2730	33098	B	2763	1	351	
2731	33099	B	2764	1	396	
2732	33100	B	2765	12	350	
2733	33101	B	2766	1	411	
2734	33102	B	2767	1	1020	
2735	33103	B	2768	72	359	
2736	33104	B	2769	1	526	
2737	33105	B	2770	1	1233	
2738	33106	B	2771	1	1563	
2739	33107	B	2772	1	246	
2740	33108	B	2773	1	747	
2741	33109	B	2774	1	861	
2742	33110	C	2775	1	1278	
2743	33111	B	2776	1	630	
2744	33112	C	2777	22	147	
2745	33113	B	2778	242	744	
2746	33114	B	2779	54	178	
2747	33115	B	2780	1	2277	
2748	33116	B	2781	1	204	
2749	33117	B	2782	1	447	
2750	33118	B	2783	1	819	
2751	33119	B	2784	1	720	
2752	33120	B	2785	1	444	
2753	33121	B	2786	1	519	
2754	33122	B	2787	1	864	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
2755	33123	B	2788	1	654	
2756	33124	B	2789	1	772	
2757	33125	B	2790	1	930	
2758	33126	B	2791	1	3594	
2759	33127	B	2792	1	654	
2760	33128	B	2793	1	444	
2761	33129	B	2794	403	1560	
2762	33130	B	2795	1412	1495	
2763	33131	B	2796	536	2770	
2764	33132	B	2797	417	1025	
2765	33133	B	2798	108	326	
2766	33134	B	2799	1	694	
2767	33135	B	2800	380	541	
2768	33136	B	2801	1	916	
2769	33137	B	2802	509	1643	
2770	33138	C	2803	40	180	
2771	33139	B	2804	1	345	
2772	33140	C	2805	170	361	
2773	33141	C	2806	1	312	
2774	33142	C	2807	307	450	
2775	33143	B	2808	1	993	
2776	33144	B	2809	1	321	
2777	33145	B	2810	1	321	
2778	33146	C	2811	604	779	
2779	33147	B	2812	52	646	
2780	33148	C	2813	7	177	
2781	33149	C	2814	118	294	
2782	33150	B	2815	337	1512	
2783	33151	B	2816	32	335	
2784	33152	B	2817	1	1026	
2785	33153	C	2818	1	1044	
2786	33154	B	2819	1	1575	
2787	33155	B	2820	1	1356	
2788	33156	B	2821	1	3726	
2789	33157	B	2822	158	627	
2790	33158	B	2823	814	3116	
2791	33159	B	2824	1	2667	
2792	33160	B	2825	1	2778	
2793	33161	B	2826	96	662	
2794	33162	C	2827	163	245	
2795	33163	B	2828	1	381	
2796	33164	B	2829	47	378	
2797	33165	B	2830	1	614	
2798	33166	B	2831	277	528	
2799	33167	B	2832	1	1059	
2800	33168	C	2833	354	491	
2801	33169	C	2834	161	466	
2802	33170	B	2835	78	2700	
2803	33171	C	2836	37	111	
2804	33172	B	2837	1	1929	
2805	33173	B	2838	36	612	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Met hod	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
2806	33174	B	2839	189	498	
2807	33175	C	2840	302	430	
2808	33176	C	2841	58	219	
2809	33177	C	2842	56	275	
2810	33178	C	2843	21	293	
2811	33179	C	2844	337	543	
2812	33180	B	2845	1	507	
2813	33181	C	2846	232	489	
2814	33182	C	2847	314	476	
2815	33183	C	2848	572	937	
2816	33184	C	2849	259	528	
2817	33185	B	2850	1	597	
2818	33186	B	2851	1	564	
2819	33187	B	2852	368	732	
2820	33188	C	2853	58	375	
2821	33189	B	2854	608	1222	
2822	33190	C	2855	41	358	
2823	33191	C	2856	73	177	
2824	33192	B	2857	1	582	
2825	33193	C	2858	1	543	
2826	33194	B	2859	1	1538	
2827	33195	B	2860	40	704	
2828	33196	C	2861	303	407	
2829	33197	B	2862	131	336	
2830	33198	C	2863	64	156	
2831	33199	B	2864	180	712	
2832	33200	B	2865	1	1104	
2833	33201	B	2866	65	228	
2834	33202	B	2867	1	2172	
2835	33203	B	2868	1	1338	
2836	33204	C	2869	181	410	
2837	33205	B	2870	1	1137	
2838	33206	B	2871	69	1322	
2839	33207	C	2872	24	266	
2840	33208	B	2873	1033	1089	
2841	33209	B	2874	367	463	
2842	33210	B	2875	1	3256	
2843	33211	C	2876	278	466	
2844	33212	B	2877	323	4268	
2845	33213	B	2878	424	1711	
2846	33214	B	2879	567	643	
2847	33215	B	2880	1	258	
2848	33216	B	2881	1	806	
2849	33217	B	2882	56	984	
2850	33218	B	2883	1	807	
2851	33219	B	2884	1	396	
2852	33220	C	2885	107	411	
2853	33221	B	2886	1	678	
2854	33222	B	2887	1	246	
2855	33223	C	2888	41	316	
2856	33224	B	2889	1	300	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Met hod	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
2857	33225	C	2890	1	273	
2858	33226	B	2891	78	169	
2859	33227	B	2892	1	882	
2860	33228	C	2893	1	246	
2861	33229	B	2894	1	639	
2862	33230	B	2895	1	411	
2863	33231	C	2896	427	522	
2864	33232	B	2897	158	826	
2865	33233	B	2898	275	310	
2866	33234	B	2899	429	933	
2867	33235	B	2900	1	560	
2868	33236	B	2901	1	798	
2869	33237	B	2902	45	384	
2870	33238	B	2903	845	983	
2871	33239	C	2904	171	422	
2872	33240	C	2905	139	360	
2873	33241	C	2906	188	436	
2874	33242	C	2907	76	303	
2875	33243	C	2908	362	574	
2876	33244	C	2909	42	347	
2877	33245	B	2910	1	766	
2878	33246	B	2911	170	1381	
2879	33247	B	2912	274	543	
2880	33248	B	2913	768	2001	
2881	33249	B	2914	140	279	
2882	33250	B	2915	1	2858	
2883	33251	B	2916	1	321	
2884	33252	B	2917	1	552	
2885	33253	B	2918	1	603	
2886	33254	C	2919	122	406	
2887	33255	B	2920	508	679	
2888	33256	B	2921	1	942	
2889	33257	B	2922	1	753	
2890	33258	B	2923	136	326	
2891	33259	B	2924	445	625	
2892	33260	B	2925	1	639	
2893	33261	B	2926	1	1850	
2894	33262	B	2927	76	1341	
2895	33263	C	2928	184	495	
2896	33264	B	2929	1	226	
2897	33265	B	2930	1	972	
2898	33266	B	2931	57	1493	
2899	33267	C	2932	207	404	
2900	33268	B	2933	664	1647	
2901	33269	B	2934	1	1305	
2902	33270	B	2935	1	639	
2903	33271	B	2936	59	1108	
2904	33272	B	2937	276	1311	
2905	33273	B	2938	1	708	
2906	33274	B	2939	123	309	
2907	33275	B	2940	1	957	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
2908	33276	C	2941	199	357	
2909	33277	B	2942	319	355	
2910	33278	B	2943	574	1044	
2911	33279	B	2944	1	426	
2912	33280	C	2945	1	381	
2913	33281	C	2946	145	301	
2914	33282	B	2947	1	1644	
2915	33283	B	2948	1	906	
2916	33284	B	2949	249	317	
2917	33285	B	2950	388	655	
2918	33286	C	2951	228	379	
2919	33287	C	2952	200	343	
2920	33288	B	2953	1	600	
2921	33289	B	2954	123	719	
2922	33290	B	2955	1	879	
2923	33291	B	2956	88	445	
2924	33292	B	2957	518	1508	
2925	33293	C	2958	1	414	
2926	33294	C	2959	202	408	
2927	33295	B	2960	1	351	
2928	33296	B	2961	1	378	
2929	33297	C	2962	84	194	
2930	33298	B	2963	1	306	
2931	33299	B	2964	238	354	
2932	33300	C	2965	326	331	
2933	33301	B	2966	1	1005	
2934	33302	C	2967	31	408	
2935	33303	B	2968	48	335	
2936	33304	B	2969	1	241	
2937	33305	B	2970	1	768	
2938	33306	B	2971	93	728	
2939	33307	B	2972	25	88	
2940	33308	B	2973	1	414	
2941	33309	B	2974	1	555	
2942	33310	B	2976	83	3457	
2943	33311	B	2977	59	1280	
2944	33312	B	2978	1	414	
2945	33313	B	2979	1	354	
2946	33314	B	2980	1	477	
2947	33315	B	2981	1	357	
2948	33316	B	2982	182	394	
2949	33317	B	2983	148	1104	
2950	33318	B	2984	494	641	
2951	33319	C	2985	44	310	
2952	33320	C	2986	303	395	
2953	33321	C	2987	229	407	
2954	33322	B	2988	195	707	
2955	33323	B	2989	713	1063	
2956	33324	B	2990	67	746	
2957	33325	B	2991	468	1010	
2958	33326	C	2992	1	258	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Met hod	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
2959	33327	B	2993	1	282	
2960	33328	B	2994	139	767	
2961	33329	B	2995	1	133	
2962	33330	B	2996	136	291	
2963	33331	B	2997	172	634	
2964	33332	B	2998	1	435	
2965	33333	B	2999	503	1294	
2966	33334	B	3000	1	495	
2967	33335	B	3001	1	1416	
2968	33336	B	3002	1	321	
2969	33337	B	3003	1	378	
2970	33338	B	3004	1	337	
2971	33339	C	3005	1	474	
2972	33340	B	3006	1	633	
2973	33341	C	3007	142	423	
2974	33342	C	3008	226	360	
2975	33343	C	3009	45	281	
2976	33344	B	3010	1	369	
2977	33345	C	3011	2082	2558	
2978	33346	C	3012	99	356	
2979	33347	C	3013	312	467	
2980	33348	B	3014	89	463	
2981	33349	C	3015	16	357	
2982	33350	B	3016	239	541	
2983	33351	C	3017	176	345	
2984	33352	B	3018	1	2238	
2985	33353	C	3019	40	309	
2986	33354	B	3020	80	835	
2987	33355	B	3021	1	741	
2988	33356	B	3022	1	1005	
2989	33357	B	3023	185	3661	
2990	33358	B	3024	1	1539	
2991	33359	B	3025	1	1197	
2992	33360	C	3026	258	584	
2993	33361	B	3027	103	905	
2994	33362	B	3028	1	159	
2995	33363	B	3029	72	642	
2996	33364	C	3030	195	424	
2997	33365	C	3031	350	454	
2998	33366	B	3032	1	1494	
2999	33367	C	3033	1	336	
3000	33368	C	3034	169	423	
3001	33369	C	3035	131	307	
3002	33370	C	3036	80	423	
3003	33371	B	3037	1	663	
3004	33372	C	3039	619	1068	
3005	33373	B	3040	1	441	
3006	33374	B	3041	1	453	
3007	33375	C	3042	174	431	
3008	33376	B	3043	236	1145	
3009	33377	C	3044	99	215	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
3010	33378	B	3045	1	675	
3011	33379	B	3046	1	479	
3012	33380	C	3047	18	272	
3013	33381	C	3048	800	1097	
3014	33382	C	3049	1	231	
3015	33383	C	3050	1	777	
3016	33384	B	3051	194	328	
3017	33385	B	3052	1	633	
3018	33386	C	3053	431	838	
3019	33387	B	3054	1	450	
3020	33388	B	3055	684	1367	
3021	33389	B	3056	112	423	
3022	33390	B	3057	28	420	
3023	33391	B	3058	28	280	
3024	33392	B	3059	1	1335	
3025	33393	B	3060	516	1396	
3026	33394	B	3061	1	1563	
3027	33395	B	3062	1	903	
3028	33396	B	3063	191	628	
3029	33397	B	3064	1	534	
3030	33398	B	3065	1	1134	
3031	33399	B	3066	1	1248	
3032	33400	B	3067	1	1479	
3033	33401	B	3068	1	1635	
3034	33402	B	3069	46	447	
3035	33403	C	3070	1	624	
3036	33404	C	3071	25	330	
3037	33405	C	3072	132	253	
3038	33406	B	3073	4	1011	
3039	33407	B	3074	392	814	
3040	33408	C	3075	414	557	
3041	33409	C	3076	74	328	
3042	33410	C	3077	1	678	
3043	33411	B	3078	1	5130	
3044	33412	B	3079	1	985	
3045	33413	B	3080	1	1671	
3046	33414	B	3081	146	556	
3047	33415	B	3082	1	732	
3048	33416	B	3083	136	753	
3049	33417	B	3084	1	1500	
3050	33418	B	3085	300	2678	
3051	33419	B	3086	1	1221	
3052	33420	B	3087	58	1287	
3053	33421	B	3088	1	933	
3054	33422	B	3089	1	1317	
3055	33423	B	3090	1	771	
3056	33424	B	3091	1	2241	
3057	33425	B	3092	1	642	
3058	33426	B	3093	1	2664	
3059	33427	C	3094	1	513	
3060	33428	C	3095	52	174	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540.217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
3061	33429	C	3096	44	428	
3062	33430	C	3097	300	437	
3063	33431	C	3098	1	576	
3064	33432	B	3099	1	864	
3065	33433	C	3100	1	801	
3066	33434	C	3101	298	480	
3067	33435	B	3102	503	720	
3068	33436	C	3103	1	756	
3069	33437	B	3104	1	355	
3070	33438	C	3105	1	1143	
3071	33439	B	3106	1	2256	
3072	33440	C	3107	537	966	
3073	33441	B	3108	1	2009	
3074	33442	B	3109	1	3021	
3075	33443	B	3110	1	1085	
3076	33444	B	3111	180	2069	
3077	33445	B	3112	1	375	
3078	33446	B	3113	31	127	
3079	33447	B	3114	47	452	
3080	33448	C	3115	149	440	
3081	33449	B	3116	119	538	
3082	33450	B	3117	1	900	
3083	33451	C	3118	1	270	
3084	33452	B	3119	1	344	
3085	33453	C	3120	72	245	
3086	33454	B	3121	1	822	
3087	33455	C	3122	69	242	
3088	33456	B	3123	2129	2289	
3089	33457	C	3124	1	255	
3090	33458	B	3125	2129	2289	
3091	33459	B	3126	1	306	
3092	33460	C	3127	1	255	
3093	33461	B	3128	82	1254	
3094	33462	B	3129	1	468	
3095	33463	C	3130	2	250	
3096	33464	C	3131	166	357	
3097	33465	B	3132	423	3286	
3098	33466	B	3133	63	436	
3099	33467	B	3134	1	4578	
3100	33468	B	3135	1	4322	
3101	33469	B	3136	46	325	
3102	33470	B	3137	58	289	
3103	33471	B	3138	1	1695	
3104	33472	B	3139	89	1195	
3105	33473	C	3140	317	541	
3106	33474	B	3141	314	992	
3107	33475	C	3142	95	222	
3108	33476	C	3143	26	172	
3109	33477	C	3144	40	255	
3110	33478	C	3145	277	508	
3111	33479	B	3146	12	1358	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Met hod	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
3112	33480	B	3147	602	780	
3113	33481	C	3148	1	306	
3114	33482	C	3149	1	771	
3115	33483	B	3150	149	360	
3116	33484	B	3151	1	567	
3117	33485	B	3152	1	345	
3118	33486	B	3153	1	1233	
3119	33487	B	3154	144	773	
3120	33488	C	3155	1	417	
3121	33489	B	3156	85	525	
3122	33490	C	3157	251	679	
3123	33491	B	3158	1	1185	
3124	33492	C	3159	541	729	
3125	33493	B	3160	211	382	
3126	33494	C	3161	200	409	
3127	33495	C	3162	85	423	
3128	33496	C	3163	243	455	
3129	33497	B	3164	152	437	
3130	33498	B	3165	1	816	
3131	33499	B	3166	79	294	
3132	33500	C	3167	6	353	
3133	33501	C	3168	82	405	
3134	33502	B	3169	3	191	
3135	33503	C	3170	204	413	
3136	33504	B	3171	75	1449	
3137	33505	B	3172	1	738	
3138	33506	B	3173	1	324	
3139	33507	C	3174	299	1009	
3140	33508	B	3175	1	447	
3141	33509	C	3176	1	570	
3142	33510	B	3177	1	703	
3143	33511	B	3178	142	744	
3144	33512	B	3179	1	237	
3145	33513	C	3180	63	254	
3146	33514	B	3181	185	330	
3147	33515	B	3184	214	1333	
3148	33516	B	3185	61	423	
3149	33517	B	3186	19	2467	
3150	33518	B	3187	4	1085	
3151	33519	B	3188	157	341	
3152	33520	B	3189	222	656	
3153	33521	B	3190	249	999	
3154	33522	B	3191	416	2447	
3155	33523	B	3192	187	1855	
3156	33524	C	3193	38	166	
3157	33525	B	3194	1	1449	
3158	33526	B	3195	286	663	
3159	33527	B	3196	255	556	
3160	33528	B	3197	85	591	
3161	33529	B	3198	32	404	
3162	33530	B	3199	185	253	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
3163	33531	B	3200	202	2862	
3164	33532	B	3201	448	833	
3165	33533	B	3202	1	1275	
3166	33534	B	3203	1	591	
3167	33535	C	3204	1	291	
3168	33536	B	3205	1	744	
3169	33537	B	3206	338	523	
3170	33538	B	3207	1	435	
3171	33539	B	3208	1	477	
3172	33540	B	3209	1	2943	
3173	33541	B	3210	1	1719	
3174	33542	C	3211	113	280	
3175	33543	B	3212	1	1092	
3176	33544	B	3213	1	1470	
3177	33545	B	3214	1	426	
3178	33546	B	3215	1	747	
3179	33547	B	3216	321	2234	
3180	33548	B	3217	1	3057	
3181	33549	B	3218	1	537	
3182	33550	B	3219	1	2496	
3183	33551	B	3220	94	273	
3184	33552	B	3221	302	1432	
3185	33553	B	3222	35	1657	
3186	33554	B	3223	2	901	
3187	33555	B	3224	82	1479	
3188	33556	B	3225	224	411	
3189	33557	B	3226	328	429	
3190	33558	B	3227	27	1098	
3191	33559	B	3228	508	1765	
3192	33560	C	3229	1	321	
3193	33561	B	3230	251	415	
3194	33562	B	3231	695	1011	
3195	33563	B	3232	1	416	
3196	33564	B	3233	45	1340	
3197	33565	B	3234	65	2087	
3198	33566	B	3235	1	1149	
3199	33567	C	3236	1	108	
3200	33568	B	3237	1	384	
3201	33569	B	3238	80	383	
3202	33570	B	3239	200	409	
3203	33571	B	3240	14	419	
3204	33572	B	3241	1	888	
3205	33573	C	3242	165	435	
3206	33574	B	3243	452	593	
3207	33575	B	3244	1472	4415	
3208	33576	B	3245	103	207	
3209	33577	B	3246	242	292	
3210	33578	B	3247	1	306	
3211	33579	B	3248	1	684	
3212	33580	B	3249	1	838	
3213	33581	B	3250	215	2593	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
3214	33582	C	3251	80	376	
3215	33583	B	3252	1	639	
3216	33584	C	3253	52	288	
3217	33585	B	3254	1	1197	
3218	33586	B	3255	39	2809	
3219	33587	B	3256	1	609	
3220	33588	C	3257	269	418	
3221	33589	B	3258	1	561	
3222	33590	B	3259	347	922	
3223	33591	B	3260	52	339	
3224	33592	B	3261	235	434	
3225	33593	B	3262	74	2676	
3226	33594	B	3263	90	675	
3227	33595	B	3264	1	1440	
3228	33596	B	3265	288	752	
3229	33597	B	3266	1	804	
3230	33598	C	3267	109	451	
3231	33599	B	3268	1	1122	
3232	33600	B	3269	1	768	
3233	33601	B	3270	380	2743	
3234	33602	B	3271	1	1296	
3235	33603	B	3272	322	591	
3236	33604	B	3273	174	464	
3237	33605	B	3274	1	384	
3238	33606	C	3275	320	385	
3239	33607	B	3276	53	485	
3240	33608	C	3277	175	205	
3241	33609	B	3278	216	316	
3242	33610	B	3279	1	921	
3243	33611	B	3280	22	453	
3244	33612	B	3281	168	817	
3245	33613	B	3282	1	477	
3246	33614	B	3283	190	1062	
3247	33615	B	3284	116	787	
3248	33616	B	3285	130	697	
3249	33617	B	3286	1	901	
3250	33618	B	3287	1	342	
3251	33619	B	3288	1	677	
3252	33620	B	3289	1	624	
3253	33621	B	3290	1	756	
3254	33622	B	3291	1	624	
3255	33623	B	3292	130	429	
3256	33624	B	3293	95	516	
3257	33625	B	3294	120	524	
3258	33626	B	3295	51	425	
3259	33627	B	3296	647	1015	
3260	33628	C	3297	518	841	
3261	33629	C	3298	67	294	
3262	33630	B	3299	1	1212	
3263	33631	C	3300	187	453	
3264	33632	B	3301	188	492	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
3265	33633	B	3302	123	647	
3266	33634	C	3303	1	219	
3267	33635	B	3304	1	690	
3268	33636	B	3305	1	930	
3269	33637	B	3306	552	722	
3270	33638	B	3307	84	304	
3271	33639	B	3308	328	1104	
3272	33640	C	3309	300	593	
3273	33641	C	3310	1	87	
3274	33642	B	3311	1	819	
3275	33643	C	3312	122	334	
3276	33644	B	3313	1	318	
3277	33645	B	3314	764	977	
3278	33646	C	3315	379	471	
3279	33647	B	3316	1	1194	
3280	33648	B	3317	1	1800	
3281	33649	C	3318	273	506	
3282	33650	B	3319	1	1689	
3283	33651	C	3320	48	212	
3284	33652	C	3321	1	507	
3285	33653	C	3322	117	251	
3286	33654	B	3323	89	845	
3287	33655	C	3324	1	651	
3288	33656	C	3325	48	212	
3289	33657	C	3326	1	864	
3290	33658	B	3327	223	839	
3291	33659	C	3328	1	189	
3292	33660	B	3329	36	144	
3293	33661	B	3330	56	389	
3294	33662	B	3331	1	597	
3295	33663	B	3332	1	606	
3296	33664	C	3333	1	426	
3297	33665	B	3334	1	696	
3298	33666	B	3335	1	417	
3299	33667	C	3336	1	594	
3300	33668	B	3337	1	228	
3301	33669	C	3338	1	879	
3302	33670	B	3339	1	405	
3303	33671	C	3340	33	152	
3304	33672	B	3341	224	429	
3305	33673	B	3342	578	4588	
3306	33674	B	3343	1	288	
3307	33675	B	3344	77	1479	
3308	33676	B	3345	132	875	
3309	33677	C	3346	120	395	
3310	33678	B	3347	1	729	
3311	33679	C	3348	8	133	
3312	33680	C	3349	171	359	
3313	33681	B	3350	1	1098	
3314	33682	B	3351	1	1547	
3315	33683	B	3352	1	933	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
3316	33684	B	3353	1	1989	
3317	33685	B	3354	1	595	
3318	33686	C	3355	62	559	
3319	33687	B	3356	1	153	
3320	33688	B	3357	1	768	
3321	33689	B	3358	1	969	
3322	33690	B	3359	217	358	
3323	33691	C	3360	449	961	
3324	33692	B	3361	1	1799	
3325	33693	B	3362	80	1327	
3326	33694	B	3363	111	258	
3327	33695	B	3364	112	429	
3328	33696	B	3365	147	390	
3329	33697	B	3366	1	585	
3330	33698	B	3367	1	2290	
3331	33699	B	3368	19	4071	
3332	33700	C	3369	1	183	
3333	33701	C	3370	1	183	
3334	33702	C	3371	44	283	
3335	33703	B	3372	1	954	
3336	33704	B	3373	1	384	
3337	33705	B	3374	709	773	
3338	33706	B	3375	1	3294	
3339	33707	B	3376	83	1229	
3340	33708	B	3377	1	1512	
3341	33709	C	3378	30	200	
3342	33710	A	3379	3	322	
3343	33711	A	3380	530	1489	YAGNESHPPSLPRYLRRSRHCGCRPPPLPVPTPTQACNAPQRRRTTSTSLACLGRAGLWLPSVSSPYLVLSSCQEQPHHCCPPSTPRPSWSPLPGMPSA/SSPGQVPAQGDLSQEDSSDSPPAEQVLPPSSGSHNTLYLGCKRFSAFILNCEPPSKLLKARPQVSELSWNPDFVAS/SAARPRDGPCSTGRQSASKTPPPPSHPHTGHSLWSEEK*KDSDSRPNQSAFPGCSVDLQFSHKLRPYLIHP/SESLGTVGNRPSQEGHELPPAPFSRMGPEQHLPVVVLPFTGAFAVVLPCPFLVSSSAWHFKVKHPSIPLLRGEK

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
3344	33712	A	3381	296	1255	YAGNESHPPSLPRYLRRSRHCG CRPPPLPVPTPTQACNAPQRRR TTSTSLACLGRAGLWLPSVSSP YLVLSSCQEQPHHCCPPSTPRPS WSPLPGMPSA/SSPGQVPAQGD LSQEDSSDSPPAEQVLPPSSGSH NTLYLRCKRFSAFILNCEPPSKL LKARPQVSELSWNPDFVAS/SA ARPRDGPCSTGRQSASKTPPPPS HPHTGHSLWSEEK*KDSDSRPN QSAFPGCSVDLQFSHKLRPYLI HP/SESLGTVGNRPSQEGHELPP APFSRMGPEQHLPVVVLPFTGA FAVVLPCPFLVSSSAWHFKVKH PSIPLLRGEK
3345	33713	A	3382	81	702	RAAFSPPAPVSSLPAPVSSPPAS TSCPPAPVSSLPAHASSPPASTSS PPAPLSSAPAHTSSLPAPVSSPP ASTSSPLVAGSGGSTTRSLPPGL GALLTHSVAPYPGGQPPPAAAD DP*TMAPAGWGSHNPRGCSCSP VAAGAGPFPASF*GPLR*AGSQ TFQILQVEVFLVVRHFSPSTP/PS VMLYPPPPSTPPTLRAPRPPIPPS P
3346	33714	A	3383	3	231	PMLLEVSVADRDAV*TFWQAPI GESQQGALGFWSKALQSSADN NS/PFQITMQPELPIMNWVLSVP SSHKMGHAQQH
3347	33715	A	3384	3	355	KIPGTSTSVKFLGVQ*CGTCQDI PSKVKDKLLHLAPPTIKKEAQR LVGLFGFWSQHIPHLGELLRPIY RVTRKAASFEWGPEHEKALQQ VQAALQAALPLGPYDPADQPL CNLNCLS

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
3348	33716	A	3385	2	1076	LCQRLLLAEPNEKPGSLGNVMAVARIEIGICEYYHEKTTEKALDSHGVLAGSTIKGVRSFQRNLELKLPATERATANAIELLTVLDQAYENFAPQILPSTGSPTSQETAQFKANQNKPLVRGKGSPHEAIRYISAAHREWKPAILTSAIRSFCSTWLVFTSKNFPKLVTQHGSTIAGNGQSSDETQVQGAAWKSDSRGTKRQIPTWILAEGNNAGAQLDIPGPTIPAPNCSLKVPQSWSTTPSMPSSLGKAYWLLACYWALVETE/RLAMGHQVTM\KPELPVMNWVLSDPSSHKVGGAQQHSINKWKWYIRNRARAGPEGTTLPLTKALTLWLKKYSNVLMLVEFTGLTMFPDILKQLE
3349	33717	A	3386	1	1416	MAQYPILDFLKVGQLLGNCALGKGNDQTFRGLLDTGSELTLIPGDPKHHCDPPVKCAAIDLANAFFSIPVHKAHQKQFAFGWQGQQYTFTVLHQGCMNSLALCHNLIQRELDCFLTPEDITLDHYIDDIMLIGSSEKEVANTLDLLFWDYRHEPLRLANYSPFERQLLACYWALVETECLMMGHQVTMRPELPIMNWVLADPSRHKVGNAQQHWKCAVHT/IIKWKWYIRDWAQAGLEGTS*LYWPRASRYQQGHQDLFILRSDLPSQVFIRDKLMERRNRRTGRTEKARIWEVTDRTVRTWIGEAVAAAAADGVTFSVPVTPHTFRHSYAMHMLYAGIPLKVLQSLMGHKSISSTEVYTKVFALDVAARHRVQFAMPESDAVAM
3350	33718	B	3387	50	693	
3351	33719	A	3388	153	578	ARIQ/GSRNQGVEVEVAPLTVTPSDPLANVLLPVPATLPSAGLEILVPEEGRLPPGDTTMMPLNWNLRLPHGHFGLLLPLNQQAKKGVAVLGGVIALDCQDEISLLLYKGDLTVMVEDKEEQNHILHGSRQREREPSKTGSPL
3352	33720	A	3389	3	402	GRHAVGDIEAEDGGGVRGPHPGGVYGLQQSHPGGGDPVWEDGHPGLPGAQQRGQ*RQQACAHHKSPSGAG*G*LPGP/AQS/AGNPDPKSPGPAPCLVGSSRNETPGAMGAPSRNGSPPTAGLGVGDGTGSPSEAV
3353	33721	A	3390	141	320	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Met hod	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
3354	33722	A	3391	1	464	HLKGLGNDTPRVCSCLIG*T*LCDCH*LQ\EASPTSVEVREPRTSVNKD/SPKSLLYSCSYSYFDEPVELRSSSFSSWDDSSDSYYETHLLHLKLV*PNLAVFNCRPTARRKPDYEPVENTDEAQKTFCKTAHNLWSLTFPFPCLL*YETRARLER
3355	33723	A	3392	3	1189	
3356	33724	A	3393	1	867	PGRPT/LSEWI/QNTLGVNVEHKTTSKASLNPRDTPPSVVNEDFLHDLKETNISYSQEADDRVFRAHGHCLHEIFLLTEGMFERIPDIVLWPTCHDDVVKIVNLACKYNLCIIPIGGGTSVSYGLMCPADETRTIISLDTSQMNRILWVDENNLTAHV*AGITGKELERQLKESG\YCTG\HEPRFPWSSSTVGGWVSTRASGMKKNIYGNIEDLEIVHFSDNDLSCIELDRLIEIVLPSSGIPLLDGYSTEIHMPVHLETSTTMCIVTPIHSSMKLETLRMSMSINCRKDK
3357	33725	A	3394	1	890	MSKSESPKEPEQLRKLFIGGLSFETTDESLRSHFEQWGTLTDCVVMRDPNTKRSRGFGFVTYATVEEVDAAMNARPHKVDGRVVEPKRAVSREDSQRPDYFEQYGKIEVIEIMTDRGSGKKRGFAFVTFDDHDSVDKTVIQKYHTVNGHNCEVRKALSKQEMASASSSQRGRSGSGNFGGGRGGGFGGNDNFGRGGNFSGRGGFGGSHGGGGYGGSGDGYNGFGNDGSNFGGGGSYNDFGNYNNQSSNFGPMKGGNFGGRSSGPYGGGGQYFAKPRNQ/GGYGGSSSSSSYGSGRRF
3358	33726	A	3395	2	441	DGMEKVDTAMNARPHKVDGRFVEPKTAVSREDSQRPGAHLTVIKM/FKE/DTEEHKLRDYIEQYG\GGNFSGCAGFGGRSGGGR*GGSGNGYNRFDNDGSNFGGGGSYNDFGNYNDRSSNFGPIKGGNFGGRSSGPYGGGSQYFAKP*NQ
3359	33727	A	3396	3	404	

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3360	33728	A	3397	2	762	MNARPHKVDGRVVEPKRAVSREDSQRPGAHLTVKKIFVGGIKEDTEEHHLRDYFEQYGKIEVIEIMT\DRGSGRKRGFVFVTF\DDP\DSVDKIVIQKYHTVNGHNCEVRKALSKQEEMASASS\SQRGRSGSG\NFGGGRGGGF\GGNDNFGRGGNFSGRGGFGGSRGGGGYGGSGDGYNGFGNDGSNFGGGGSYNDFGNYNNQSSNFGPMKGGNF\GGRSSGPYG\GGGQYF\AKPR\NQGGYGGSSSSSSY\GSGRRF
3361	33729	A	3398	1	3737	
3362	33730	A	3399	5	633	DLREWSWARRTAWEPRGKRVRGK*AFKEIQCP*QQKE/SMSGLLLLKVVAKEMTWLPPLSAIQAPGKVEPTKFPFPNKLMFSWWYIETTTASAKVIGYKPSVLNCATLRVQIMSHYHSYRHLASLLVEGSATLPGHSHILGPLIRHPDKVSAGKPRVLGLQLLKEDCSSQPAAKPQGPHRLCSSLILHRARARLGPEQ<RETKVPFSKGTTH
3363	33731	A	3400	2	816	QVPTMVDWAGWSPGLWTTCSGTGGGGAEQGWANWSLVLPGVLAGTSLETFSPLS*GLTFSSLLLMQISAASLNFSSENGIFFSTTLPGCKFSKFLCSASLLKWNAFSSTQVTS*MLCCSEISSTRYPKSSL*SSKFHKSLEQGQNAASLFAKT*QESPLLQLPTSSSSPSETTSAWISLSISLSVFLSKLFDKSLESSKLS\TFSSVLLSPPNCSNLCLLPSFKVACTFLGTFLRSTSLHWYQFTVLVCFHPADKDILKSEKKKRCKEK
3364	33732	A	3401	1	485	LFKAVLHDPHLKLLSLYGTSLSHTDVSHLCETLKHTTCKIEELMLGTCDISDEGCEDIASVLACNSKLIHLSLVENPEKDKRM\CCCALETLMLMYCCLICVSCEDISHVLFCSKSLSLLDLGSNFLEDNEV\HLLCEALKH*DACKTWRSLNFDWVGYLGC
3365	33733	C	3402	952	1164	

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3366	33734	A	3403	3	163	IAVSKQDPITSLEQEKEPWNMKICEMVDESPAMCSSFTRDLWPEQDIKDSFQQVILRRHGKCEHENLQLRKGSASVDEYKVHKEGYNELNQCLTTTQSKIFPCDKYVKVFHKFLNANRHKTRHTGKKPFKCKKCGKSFCMLLHLSQHKRIHIRENSYQCEECGKAFKWFSTLTRHKRIHTGEKPFKCEECGKAFKQSSTLTTHKIIHTGEKPYRCEECGKAFNRSSHLTTHKIIHTGEKPYKCEECGKAFNQSSTLSTHKFIHAGEKPYKCEECDKAFNRFSYLTKHKIIHAGEKP\YNCEECGKGFNWSSTLTKHKRIHTGEKPYKCEVCGKAFNESSNLTTHKMIHTGEKPYKCEECGKAFNRSPQLTAHKIIHTGEKPYKCEECGKAFSQSSILTTHKRIHTGEKPYKCEECGKAFNRSSNLTKHKIIHTGEKSYKCEECGKAFNQSSTLTKHRKIHTRQKPYNCEECDNTFNQSSNL/N*/HKIIHTGEKLYKCQECGKASKQSFTLTKH*ILFNK
3367	33735	A	3404	3	345	
3368	33736	B	3405	282	694	
3369	33737	A	3406	586	1403	VSETALADGRCWFRKCQSHLCLASTTGKC*TSTLQSGRDYTENGESAQEGETGLPERRLAHCT*LAEVHRRQPD*TQENRP/SKMGIMTSS/AAKDHLDNKCQRQDSIPGSSRGPSPLTMGAQDTLPVAAAFTETVNAYFKGADPSNTPSVLVEQLLSKRRSNPIMDHGGHKVPCSLPPLLTHPNRRQRELKMYGSHKAVAQPSPLQDRLQQCAVPTPVTGWTNSRAALGDIFSTWGSLLLRTSTPKKAAARARPMCPCPGAYNTSYPLAPYFWR
3370	33738	A	3407	1	421	FRHSMNGCEKDSSSTDSANEKPALIPREKKISILEEPSKALRGVTGPNIEKSVKDLQRCTVSLTRYRVMIKEEVDSSVKKIKAAFAELHTCIIDKEVSLMAEMDKVKEEAMEILTARQ\RKAEALKRLTDL\AS\QMAEMQL
3371	33739	A	3408	1	403	MEILTARQKKAEELKRLTDLASQMAEMQLAELRAEIK/*WFSENELGNSDLCSYSCYCLAAQKLSCQCYLGGTAHSAPGIAKRKTSQLI*PLP

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3372	33740	A	3409	1	756	
3373	33741	A	3410	2	1849	QRRRRNTPGWSGFQGLTRAPALFPRLIFQSSSETRLLSGTLLWIPRAYSTRSKMAELNTHVNVKEKIYAVRSVVPNKSNNEIVLVLQQFDFNVDKAVQAFVDGSAIQVLKEWNMTGKKKNNKRKRSKSKQHQGNKDAKDKVERPEAGPLQPQPPQIQNGPMNGCEKDSSSTDSANEKPALIPREKKISILEEPSKALRGVTEGNRLLQQKLSLDGNPKPIHGTTERSDGLQWSAEQPCNPSKPKAKTSPVKSNTPAAHLEIKPDELAKKRGPNIEKSVKDLQRCTVSLTRYRVMIKEEVDSSVKKIKAAFAELHNCIIDKEVSLMAEMDKVKEEAMEILTARQKKAEELKRLTNLASQMAEMQ\LAELR\AEIKHFVSERKYDEELGK\AARFSCDIEQLKAQIMLCGEITHPK\NNYSSRTPLQAPCWPLLNA\HAANLWGKQSNF\SRKSSTHNKPSEGKAATPKMVSSLPSTADPSLRAMPANKQNGSSNQRRRFNPQYHNNR\LNGPAKSQGSGNEAEPLGKGNSRHEHRRQPHNGFRPKNKGGAKNQEASLGMKTPEAPAHSEKPRRRQHAADTSEARPFRGSVGRVSQCNLCPTRIEVSTDAAVLSVPAVTLVA
3374	33742	A	3411	1	489	MAEVQVPVLHGRGHLLGRLAAIVAKQVMLGWKVVVVRCEGINISGNFYRNKLNCSFRTPSCIFRWTVRGMLPHKTKRGQAVLDHLQVFDGISPLYDK/K/KRMVVPAALKVVRLKPTRKFAYLGRLAHEVGWKYQAVTATLEKRKEKA*IHYRKKKQLMRLRKQA
3375	33743	A	3412	2	260	
3376	33744	A	3413	1	612	AEVQVLVLDGRGHFLCRLADIVAKQVLLG\RKVVVVRCEGINISGNFYRNKLKYLAFLRKRMNTNPSRGP\YHFRAPSRIFWRTVRGMLPHKTKRGQAALDRLKVFDGIPPPYDKKKRMVVPAALKVVRLKPTRKFAYLGRLAHEVGWKYQAVTATLEEKRKEKAKIHYRKKKQLMRLRKQAEKNVEKKIDKYTEVLKTHGLLV

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3377	33745	A	3414	734	1488	MTKDPWLKQSGSSDTSPAASPGHFRAVPRAPRARGTVVHHRH/LCLSSWPSSS/RVPPGCASYTPASTAAGALPYQAQRRQGVLRRYTTYLRV*HFLPRGLPEGFQRGPRVPPPPPCPMAAEPELGHALKLLD\LREIVSFLYYFFFFFLRRSLTLSPGWRDLGSLQ\PLPHGFKAIF/SCFSLLSGWD\YRHTATHAQLIFVFLVEMGF/TPMFARMASIS*PCDPPDSASQDAGITGVSHQVWRERLFLDEGGGGCP
3378	33746	A	3415	48	966	WSQVVTIVTVVVTVSGSNHGNHTQASHEGYRHPMRAQVSH/GECR/PSHEGHRHPMRTQASHEGHRRPMRTQASHEGHRHPMRTQASHEGHRHPMRGTGVP*EHRHPMRAQASH/GEHRR/HH/GEHSCPMRAQASHEGTGVP*EHRC/HHENTGVP*GHRCPMRMQASHAGHRHPMRVQASHEGHRCPMRTQVSHEGHRRPMRVQASHENTGVP*GAQASHEGTGVP*EHSHPMRAQASHENTDVP*GVQASHEGYRRPMRTQASHEGHRCPMRAQTSHENTGVP*AAQYRP*EAGAPQGGQGWQETGADRST
3379	33747	A	3416	8	432	NSKLPPVVTSQQMRFMY/DPQTDQHMKI\FPEQLPLDEFLQKTDPKDPANYILHAVLVHSGDNHGGHYVVYLNPKGDGKWCKFDDDVVSRCTKEEAIEHNYGGHDDDLSVRHCTNAYMLVYIRESKLSEVLQAVTDHDIPQQL
3380	33748	A	3417	38	2865	SFRWDSKKHTGYVGLKNQGATCYMNSLLQTLFFTNQLRKKLLMGALPWEGALAPWV*ALDTDPSLPCSTCLTTARTCTSL\QQCHADQCRWQTRWQGSSRW*WQQEEIGQEREEGVEYAKRVLLGPPYSISDCTHMESSLPPCSS*DPGSFQFHEERAEDEKSEGRGPSCSCTQPPPW*SLGEGLGECR*ESSSSYCSLAGLSLHP*ETRGERLQEASQGQPESPFGEV*HPALVSLDLAE*QGRAEKHGCTETH

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3381	33749	A	3418	2	3515	YVRVSLPPPPPAAGRPGAAVADDAREEEEEAAPPPPPPPPPRLAAARPPGSQPRPPAAGEAQAAADMNHQQQQQQQKAGEQQLSEPEDMEMEAGDTDDPPRITQNPVINGNVALSDGHNTAEEDMEDDTSWRSEATFQFTVERFSRLSESVLSPPCFVRNLPWKIMVMPRFYPDRPHQKSVGFFLQCNAESDSTSWSCHAQAVLKIINYRDDEKSFSRRISHLFFHKENDWGFSNFMAWSEVTDPEKGFIDDDKV
3382	33750	B	3419	36	335	
3383	33751	A	3420	2	1602	CRLKTTAFSSPSSRHITACLPRFWQICSLPKHLIPPEAPPVGMS*RRRKPVWVKSMMLG*RIP*GKRDPPTTAKCRTCSPQEETGPAGTQGQAARQLERRKLPPYVQT/PPRPDQLKGVCSLQTDAISLAPTAERHSRLLPPPSRQQPTSAGTEAGACPNTRRPSGLQLPAAV\QTPSGQTPSVPKPGLEPTSLPVGSG/PISASHSQ/PVSKINKK**VCESPYMETFP*DAKRTRHKRADTARRGEPLRPRTSVPRRTVPAPSEKLRGSRRGEPTPAAPRRDPRRAGSLTHAGPPGG*RHR*PGWPRGTA/AKTPVAAEALIAAAAPLALHRIPLGAPPQLPAAPAP/RLALALRGASAA/RPRVAPSAASPQRCLLR\GPPSPQPSPAPGPVAPSAQGRGAVPGGVLAVLLPGAPRLSGKRPAAPRGGDTPAQGQVPLAARAPREGPGHGREPVIEELERRGAELRSGKGGTRSEGVRGGRARGIVYGGAHGPEVGKDKMPLKPRNLSAPVAIGGLLHGAGIRFLNLALHSPAVDFGQIT
3384	33752	A	3421	3	498	IIDPTQYRPMVPNKVSSPC*WLPTITQVHPDNEAEPIPS/PARSCAPICGVP/AYGSPLSQSSVS*TRQ*FPSCSQSL**GSPTLVNPKTAYT*NSGSRGG/VSFDEDTSQHCYPGTG*GQQPLQ*SRNHAGPPGG*MT*VTGVAERDK/PPKTPVGRRGTHSQPPRRSP
3385	33753	A	3422	1	270	

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3386	33754	A	3423	1	1899	MGFCHIGQAGLKLLTSKDLPASAFQSAGIAGFWLLDGISGPILGQREACCPAGNSNKELKQENSALAEQLQVVLIDKAGMQCDLEELKKKLELTELTLQQLSSWCEAPDANQQLQQPTDERAQLEAHLGQVMEWLKYLQMEREQYAEYLHGESAMWWQRMREMSEQIGHLIVPGICEMGGAQPEVVMGLGFVEVHTLREERVHSMSRVQELETILAELRNQVAEPLPPEPPAGPSEVEQKLQAEAEHLWKELENLAGQLQAQVEENEGLSHLNQEQE\GLLRLLEQEEKLLEQEERLLEQEERLLEQEERLLELQESLLEQKRKAASFLS*TPTPGAPSRALRGKYVTSYQSQRSV/REDVDRENEYISRLAQDKEEMKVKLLELVLQLVGDCNKWHGRFLAAAQNPADEPAPWDPAPQEIGAANKQGGLFPGCCLVTPGGFHGDCRGAYGAQSSPDSQQAQNPDLAVAGKAAFWEFKEHQESLTLLKSWGRRKSGSGQAAQLREGSRCAAARRHLARALPAARMPKRKVISTEGAAKEEPKRTSASLSAKPPAKVEAQPKKAAAKDKSSDKKTQTKGKRGAKGKQAEVANQETKEDLPAENELSSLYSFYARSLILAFIIHLRM
3387	33755	A	3424	198	364	FLII*YEGINCSRIVNLTRTAWCFFSG*IFRQKKCKQKGKGEQRENRPEVANPRN
3388	33756	A	3425	3	238	GVCPPRGRSCSDFKADSLYSFPCPSRCGS*ESSTQTCSGFWTGCTALHRWRGMPERCPPESRDS*TRFPQSSLPGHKT
3389	33757	A	3426	3	681	HIRGPRYSGHHSAFGCPYSDMNLKKEATLHDRLREQTQAN\LESDSSHSKSKSLCSLNFNGKHEKVNSQPRLVQQAKCLKIKGKEDIDLDNLFREYSVEQAQQVLHQSVSMSTVSAHPFRDLPLGREQHCKLLPGVADIRASQVARWTVDEVAEFVQSLLGCEEHAKCFKKEQIDGKAFLLLTQTDIVKVMKIKLGPALKIYNSILMFRHSQELPEEDIASGQEVRG

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3390	33758	A	3427	30	981	TQDPWPSLPVLWSRASSDPAAGHRAEHI*TYWPWKLEGT\DIWLVLYMPLVQPDNFIKKHSHLPTYCLFKEDVKFPFRTCRLTYCWLNYTEEITYLHTKKVSVGQSAVREEFAAACTWSIRIGEKLAILLSLYLCRQQALLNMRMSVPIHESGVAQRSPVMDKLAQYSVEQAQQVLHQSVSMSTVSAHPFRDLPLGREQHCKLLPGVADIRARQVARWTVDENLHGLIQTKQTPHLDESISKGESPALVVTELRMCMTATEPLVPTKNPYQERGHIGDSFLHYTDQEPQPWDQSSVHPTPAPIYSVSSGFRVTRGSDI
3391	33759	A	3428	1	864	MVSALPEVGRAQILRLIAYIRSPAPPVVGVERAARRPAQAFGLVALPSTDATVFANQPLARACIGAARHREPDAPGQSAWVGEECLKDALRSPETPKLGSLSPPCQDTRPGRASNDFSLEMGYSSLSAARLKIHGQVFQCCGPGPLRTL\HWTQS*TYLNILALET*GAQNQP*EWQAVD*GAPGLFSHTLGVFPR/RLPQHPKQIICFQNYEYSVEQAQQVLHQSVSMSTVSAHPFRDLPLGREQHCKLLPGVADIRASQVARWTVDEPYSSAPRGPELSAGANSSRGA
3392	33760	A	3429	201	336	QQTPGKAVHAPFIADQSLT*ELVSVFPQFQLFPYRR*DSHSGKS
3393	33761	A	3430	600	768	TDTSSYHGSG*PAR/NG*MHSFIRCLLLK*GIEPCALNGDSVLKSRTDVTFTPVNITTKVKSVEMHNEALSRALPGDNVGFKNVSKMFVMATLLFSDCIHNTFDQMWRTKEHNEARWSLQSSGDKVMKENDELRDSVSQLQKQTLSLKSPKIALGESLISCRERAEIEIVDKQTQALIMGVADLQGRVNAQLHQVSTVKVRDWKRMGPYNLECGTVGRTLIKLWTLSL
3394	33762	A	3431	1655	1841	EHQAEAEGGDGGPRSLPMKPGSPLMPDKAQRKQVRSRHGRGGRGGG*AGPGIPGKPGSPVSP
3395	33763	A	3432	1	1773	

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3396	33764	A	3433	648	1884	LDPEVAWAKWQHSTVKGPQKQFAFSWQGQQYTFTGLPQGYINSLSLCYNLIPRDPD/RL/SLLQNITLVHYIDDIMLIGSSEQELAYTLDLLVRRLCAKGWEINLTEIQEASTSVKFLRVQWCGACQDIPSKMKDKLLHLFPPTTKKKASLFGFRRQCIPHLECGPEQEKALQQAQAAVQAAVPLERYDPADPMVL/V/ELTWLWPLLSAQFASSGDQH*ALHMAPFLGVVSQLPGGKLIILDIFHHGKGRVLFSLE*TLTPDMGLPILHIMLLPRLPSVNSQNALSTVMPGFTGPGIKGWKWHHSPSPLVIH*QNFCFLFP*HYVLLA*RS*FQRKEPCHQET*Q*FH*TGS*GCQLDTLGSCYF*VNKLRRELQCWLG*LTQTIKMKSVYYSITENCWMKRSPVKRRKILELEEA
3397	33765	A	3434	1	2223	
3398	33766	A	3435	1	1078	MNKEMSGQTFVGKQNSVRMPKIISGLGVQKPNRQWRLVQDLRIINEAVVPLYQAVRNPYTLLSQIPEETGWFTVLDLKDALFCIAVHPDSQFLLAFEDPLNPTSQLTWTVLPQGFRDSPHLFGQALAQDLSQFSYLDTLVLRYVDDLLLAAPSETLCHQATQVLLNFLATCGYKVSKLKAQICSQQVKYLGLKLSKGTRALSEERIQPILAYPHPKTRKQLRGLLGITGFCQIWIPRYSEIARPLHTLIKKTQKANTHLVRWTPEAEAAFQVLKKALTQAPVLSLPTGQDF\SLYVTEKTGIALGVLTQHYGEERNS*LPTEYLSNIRKPLGDYYWLYRNLKRWQSYTARVIRKERKGK
3399	33767	A	3436	1	1677	

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3400	33768	A	3437	1	2052	MVLVVVAVVVVVLVVAVIVV VVVVVAAVVVGAVVVVVVVV MVVVVVVVVVEEDNQHKTGA INNNNTAKNPQQSPFHSPATST GAEATQMRRNQKTNPHNMTK QVSLTPPKITLAHQQWIQTKKK YLIYLKKHSGVNKIPRNPTYEG CEGPFQGELQTTAQQNKGGHK QTEDHSMLMDRKNQYCENGH TAQAVPNPYTLLSQIPEDAEWF TVLDPKHAVFCIPVHPDSQFLF AFEDPSNPMSQLIWTVLPQGFR NSPHLFGQALAQDLSQFSYLDT LVLRYMDDLLLATHSETLCHQ ATQALLNFLATCGYKVSKPKA QLCSQQVKYLGLKLSKGTRTLS EERIQPILGYPHPKTLKQLTAFL GITGFCQIWIPRYSKIARPLNTRI KETQKANTHLVRWTPEAEVAF QALKKALTHAPVLSLPVGQNFS LYVTEK\TGIALGVLT/PGTSAQ LAELIALTRAPELGEGKRVNIY ANSIGREREFLTSKGTLVKHQE AIKRLLLAVQKPKEVAVLHCW GHQKGKEREIEENRQADIEARR AARQDPPLEMLTEGPLAFELA MATARAELSLAIHHCCLPPPPQ TRCWLPSLRIRQGVCCIPDPAR AITLTAWPKIPFLGIRKAKNPRS EKTRLATILEAACCHFGSGPPPS WELWEQGPPVTVQTHILRSHL

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3401	33769	A	3438	294	2340	EKCRHNCSSRVWQSLVSQSVW ATEGQYGRTKNARPVQVK\DS ASFPYQRRYPLRLEAQQGLQKI VKDLKAQGLVKPFNSPCNTPIL GVQKPNGQWKLVQDLRIINEAI VPLYPAVPNPYTLLSQIPEEAE WFTVLDLKDAFFCIPVHRESQF LFAFEDPSNPTSQLTWTVLPQG FRNSPHLFGQALAQDLSQFSYL NTLVLRYLDDLLLAAHLETLCH QATQKKTGIALGVLTQVQGTSF QPVAHLSKEIDVVAKGWPHCL WVVAAVAVLVSEAVKIIQGRE LTVWTSHDVSGTLTAKGDLWL SDNLLLNQALLFKRPVLRLHTC ATLNPATFLPNNKEKIEHNHQQ VIVQTYTIQGDLLEVPLTDPDL NLYTNGSSFVEKGLRKAGIHPS RQWTPLWPKAGPEMLSKRQVL ESGILKAFLVPYLLVAVLGSIDF NGKPPVAVFSLSQAHRFLCAT WLLLGYGEVWIHSHTAIKTYQ RRRSQDGRIGTAPVYSSQRERR RRRVISAFPSEGIPTDLQLRVLS VRRKTNKQKGHPHQKPICTSPS SRPKVDKTTKMGKKQNRKTGN SKTQSASPPPKERSSSPATEQSW MENDFDELREEGFRRSNYSELR EDIQTKGKEVENFEKNLEECITR ITNTEKCLKELMELKTKARELR EECRSLRSQCDQLEERVSAMED
3402	33770	A	3439	2	350	YKVSKPKAQLCSQQVKYLWLK LSKGTRALSEERIQPILAYPHPK TLKQLRGILGITGFCRIWIP\R*S SPTGQE/FSLYVTEETGIALGILT QVQGTSLQPMEYLNKEIDELDQ GRTH
3403	33771	A	3440	1	897	
3404	33772	A	3441	1	429	

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3405	33773	A	3442	3	957	NKIPRNPTYEGCEGPFQGELQTTAQQNKGGHKQTEDHSMLMDRKNQYCENGHTAQAVPNPYTLLSQIPEDAEWFTVLDPKHAVFCIPVHPDSQFLFAFEDPSNPMSQLIWTVLPQGFRNSPHLFGQALAQDLSQFSYLDTLVLRYMDDLLLATHSETLCHQATQALLNFLATCGYKVSKPKAQLCSQQVKYLGLKLSKGTRTLSEERIQPILGYPHPKTLKQLTAFLGITGFCQIWIPRYSKIARPLNTRIKETQKANTHLVRWTPEAEVAFQALKKALTHAPVLSLPVGQNFSLYVTEK\TGIALGVLTQELVLSWQN
3406	33774	A	3443	146	1303	EKCRHNCSSRVWQSLVSQSVWATEGQYGRTKNARPVQVK\DSASFPYQRRYPLRLEAQQGLQKIVKDLKAQGLVKPFNSPCNTPILGVQKPNGQWKLVQDLRIINEAIVPLYPAVPNPYTLLSQIPEEAEWFTVLDLKDAFFCIPVHRESQFLFAFEDPSNPTSQLTWTVLPQGFRNSPHLFGQALAQDLSQFSYLNTLVLRYLDDLLLAAHLETLCHQATQKKTGIALGVLTQVQGTSFQPVAHLSKEIDVVAKGWPHCLWVVAAVAVLVSEAVKIIQGRELTVWTSHDVSGTLTAKGDLWLSDNLLLNQALLFKRPVLRLHTCATLNPATFLPNNKEKIEHNHQQVIVQTYTIQGDLLEVPLTDPDLNLYTNGSSFVEKGLRKA

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3407	33775	A	3444	1	1647	MNKEDYNDDDDNGDIKYLPDIKTGYNKTVQIPITSENSTVGLSNTEADEMDRLKCERDDALKEVNTLKRRTKGGKHLTLKVTYTLSETNLHKNYLWECILMGQLGCYEILRKPSPALGLTPEHKGNVGHTGEKTGAG/PATSRPPDSFPN**GPPFNPNGTKGDRQRGKQQTKECQYSPIMPTPSSGRRRIWSSQ\RHVPFSLSDLIDLAVPNPYTLLSQIPEEAEWFTVLDLKDVFFCIPVHPDSQFLFAFEDPLNPMSQLTCTVLPQGFRDSPHLFGQALAQDLSQLSYLDTLVLQYVDDLLLAACSETLCHQATQALLNFLATCGYKVSKEKAQLCSQQVKYLGLKLSKGTKALSEECIQPILAYPHLKTLKQLREFLGITGFCRIW/NFQALLLERPVLQLCTCATLNPVTFLPDNE\EEYNCQQIISQTYATRGDLLEVPLTDPDLNLYTDGSSFVEKGPQKAGERRAVLASQTSLTPLGRNGRSIPATLALESKELVKSVRALLDMDCAIPFLVGTSIVDPYLKYEPTTKNHLIMVQGEKNCITGR
3408	33776	A	3445	1	2217	
3409	33777	A	3446	1	749	MNQSDQEMTGAFVHMKSYTGLISGVAVKMERHIYQDRRIAIEKEFNSCRTGCMGDWSFTITQIRLLENTGIRVFKDNLVEEAEWFTVLDLMDAFFCIPVHPDSQFLFAFEDPSNPASQLTWTVLPQRFKNSPHLFGQALAQDLSQFSYLDTLVLRYMDDLLLAAYSETLCHQATEALLNFLATCGYKVSKPKAQLCSQQVKYLGLKLSKGTRDLTTFLPVNEEKIE/P*LSTSNCSKLRCSRGTSRGSLG

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3410	33778	A	3447	1	1374	MPLLQMIATPLQQSLISTEDEM DELTEVGFERWVITNFTEEPSPA LGFTPEHKGNVGHAGKGPLESS SPDPFLCGQEKQEKGAGLLHRQ YPLRLEAKQGLKKIVKDLKAQ GLVTPCSSPCNTPTLAVQKPNG QWRLVQDLRIINEAVVPLYPAV PNPYILLSQIPEEAEWFTVLDLK DAFFCIPVHPDSQFLFAFEDPSN PMSQLTWTVLPQGFRDSLHLFG QALAQDLSQFSYLDTLVLQYM DDLLLVTHSETLCHQATQVLLN FLATCGYKVSKLKAQICSQQVK YLGLKLSKGTRALSEERIQPILA YPHPKTRKQLRGLLGITGFCQI WIPRYSEIARPLHTLIKKTQKAN THLVRWTPEAEAAFQVLKKAL TQAPVLSLPTGQDF\SLYVTEKT GIALGVLTQHYGEERNS*LPTE YLSNIRKPLGDYYWLYRNLKR WQSYTARVIRKERKGK
3411	33779	B	3448	1	2862	
3412	33780	B	3449	94	1248	
3413	33781	A	3450	1	3805	MQWEEAEKDPSGSCVFQRPPV ALVFPLHSKWTLVNSPPSSGDP YVPGRPAQSGQLSLSPAPPYVL PGPGKIKQAGNNPSLTSIYRSEV FCAHRHLHPPQLVCARGHIGSA HLSVDRGSLIWEVLESTVWART NEWSPVTRTVLISALASTHIPQP CESRPPVPPEYEVTVLRSQGTA QLPPWSSSTSWRLTDPSCPKHA AWLTDLASSKGPAAGGTGSFS QPGTLTSTRTNPLKKEKSPEDL KQIKIDLGKFSDN
3414	33782	A	3451	1	444	YSLVEFHTLVLQKSDVEAVF/S KYCFIVGCSVHKGFAFV*YVNE RNARAAVGGD\DSSSFDLDHDF QRDYYDRMYSYPAHVPPPPIAR AVVPSKCQHVSGN\RRGKSGFN SKRGQRGSSKSGKLKGDDLQAI KKELTQIKQKVDSLLENL
3415	33783	A	3452	3	93	
3416	33784	A	3453	117	316	SSATFSAL*ETLPSNTMASSSFD LDYDFQRDYYDRMYSYPARVP PPPPIARAVVPSKRQRVSGNTS

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3417	33785	A	3454	102	1059	ETLPSNTMASNVTNKTDPRSMNSRVFIGNLNTLVVKKSDVEAIFSKYGKIVGCSVHKGFAFVQYAYE\RNARAAVAG\EDGRMIAGQ\VLDINLAAEPK\VNRGKAGVKRSA\AEMYGSVTEHPSPSPLLSSSFDL\D\YDFQRDYYDRMYSYPARVPPPPPIA\RAVVPSKRQRVSGNTSRRGK\SGFNSKSGQRGSSKSGK\LKGDDLQ\AIK\KELTPDKTKKWDSLL\ENLEKI\EKEQSKQAVEMKNDKSEEEQSSSSR/VKKDETNVKMESEGGADDSA\EEGDLLG*MNDNE\DRGDDQLE\LIKDDEKEAEEGEDDRDSANGGG
3418	33786	A	3455	299	509	
3419	33787	B	3456	16	101	
3420	33788	A	3457	1209	1828	GNCDSPARPARPPHRQGCPRPSPPPRGRPRALGPTRASAARAPADLPPPAAPHPAPAALVPHTAAPKA\RNALPGSPGALTEGAVLLPNAGARPRRPRSSEKP\GPAPSWPRIPGFRTGAPPPATPVLAAGGLAPPSPGLAGQQVALPSQVPADTQSGVKSGSQDRGRN*QSAGSAGGGARTQVPGPLRMWKRAVWPGDWAPHPANI
3421	33789	A	3458	387	772	PHRKQAEPPRHHERLGRRVRHHARHGRGSRPDTAAEAAGGCGDPRAFQQLERRLRHPPLRWQGLLRRQRLLREEPRRSLL/QTS*S*CSPVTRPSSGCSSPRSWMETRRGAPAPPAPRSRNKPTTWWPH
3422	33790	A	3459	362	608	FFFFFLNRVLLCHPG/WS*SGNHQWQSWLNS*PQTPGLK*SSFLCFRKWWDYKHEPLYPAKPHFEFLFGSSLQVREFFGKIKV
3423	33791	B	3460	1	612	

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3424	33792	A	3461	1277	2152	SRAAPTCFSWLPCGASTCPWLMWAMSGRMVAPLQRVLRAAPGLEGTLGGRQHPGTPPSVLHFSLTMNSMFGLQDFNVTPLAAQATLPPGSPGRPTLVPSTAAPNSLQMFTGGHGA*FPRWQPQPPSGVS/SHGAPPGVPHYCRQGRSPGKR\QRKWLESEVQAQGP*EPDPTQLQTSTRTACG*GPPSQADPDPDPTRPRTPDLDPNCMRLRTPKPGRRQSRPH\GPRTPTQTDPDPPVQPPAPEVKPQRPP/WAARAPSDTAAS*GGLTCNSRPIREGQMGSPSPAGSLLLGAL
3425	33793	A	3462	1	2064	MDGQCSHYCVKTDLRVHSPFTTGAVHADQSCCKTTSARWEDTCDLTGSKKTLVISNIVIRTRSDDKLENEWETQSQNRNRVKPTAADPCRNE/NEHSS*EKHPEVLQESANDRLRDNERVSQRQSQPTTVSQRQSQPTTESEPTTES/RQRQSQRQRQSQPMTESETMTELQKMTESANDRVSQRQSQSQRQSQ\QRQSQRQRQSQSQ*QSQSQRQSQSQRQSQ\QRQSQSQRQSQ\QRQSQRQRQSQRQ*QSQSQ*QSQPTTESEPTTEVSQRQNQRQRQSQP/DDRIRDNDRVSQRQNQRQRQSQ\Q*QSQRRQSQSQRQSQPTTESEPTTESANDRVSQRQSQSQRQSQ\QRQSQSQ*QSQPTTESANDRVSQRQSQSQGQSQSQRQSQS/DDRVSQRQIQSQHQEDRPPKYQNKNVQVHA/DDKPRSDPQRRRNLTPPVKTAERRPHQEHVVKGEKATSPSRHSTSTAPTRPPSAETAHVNVMCGGDMAHINQGHVEAPQGSHEKHVGAARDQYERRDAQSEKSQQVQTTGLRVHVSRRPPHDGSLTSTGLRVHVSRRPPHDGSLTSTGLRVHVSRRPPHNGTVTSTGLRVHVSRRPPHDGSLTSTGLRVHVPRRPPHDGSLTSTGLRVHVPRRPPTTALSHPLDVSICRTLNAYPEMLTGERSTFPCVNVKNEKAVESKKDTPFKCESKESWI
3426	33794	A	3463	1	424	

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3427	33795	A	3464	1	492	MDESSFRGSITQSGSAKTAGLTGFCKLCKTSSWHTGAAQILEGGMEKANSPQYADPQTHLSWHTLPPGSQATSANESNVNFLSLPDTNSPEIRPDHSPPVPDRSVSPLEHIPRTFPKPGTG/PPHINTVTNPSAGAPR*E*PS*SGFNPGCFQLVRPSRISGTPV
3428	33796	A	3465	107	543	KREGWKEESDFWDGSHLPPLNSRCSTRKGRKTGRCGAATAAASSPREGRRPPPSWAGHPCLGSCQWLRSCR/RGLAMAPGALPALGEEEGPGASGLSAEL/RASERGLGQGLGPAALHS*ASPTPWAPVRPEPPRRAPPPAPWRPVPL
3429	33797	A	3466	27	1021	STQTWPVSEETGSPPQRNRC*SSHQPDTASWVLQREYSHRKGTAPRGMQGTLPLCPSLSGCRSPSCPAAARPPRPRAVRFPPPATAAASSPREGRRPPPSW/RRPSLPRGLPVASELPEGLAMAPGVLPALFGSTLPL*AVT/PH*ECL/PASLLKPARP*THREK*TTPDVQP*EL*HSP*RSAASLQEGPQLHS*SQ*DQEPTNSGHTYTLGTGR*FYTVCQFLWLG*TYRSSHRPGFACRCLEPGSAAPCPSHCLSAGPEGTL*AACLGKVPGRSAPRSDQWSPGGRAPRGVPPPPLSRGHCKALASCAPSADA\REPPHRALLGSPKVHTP
3430	33798	A	3467	807	1428	GSDRLQPQPLLFGRDVLLLLPSGPAIPASGLASVFGAAGRAGHGSGGSA*TWGRGRTRRERPLGGAGASE\PGSVGPRGA\GWVSGPVRAPPRAAPGTLAPSSGRCRAPPPRRAQACVALTCPGPGGRCPLPMDRPALAMP/SHL/HPRPGQVAPRWSPCSRRREEKGRHERVDIGHSHLVFALTLFLP*FGGGGKTEAAQNSWRIPPAG

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3431	33799	A	3468	68	1153	LLKMFRAKAACLTSMAWVLPPLSLIVLVILSPGSFILQITFTLLEPVLRRPSSAEKPLEPGPSSSPSSGRARGA\RPALPAAPKPLASPEAGMAVPGWGRR\SPSRREEAGAVACLSLTVFSGKWICQQAP/SAWGCCC*D*GKLVHRST*RCAR*KYPGLKPDQEGYCQPGAPVEVHPRCRDFPS/VLRRNLGFSALAQSEYLW*DHS/CVLVVG/PVLFC*TLFASFPIRLYPEELLA/HKVTQCPSLVSPCNWLSAGGGRKFEPALRRPSSAERPLAPYPSSSPGAGRAPQPWPALPAAPKPLASPEAGMAGPGGRRTTSLPKRRGCGCSRPASSCFSSLSGWAARVERRQMASIPEIALLFPSPL
3432	33800	A	3469	1	248	FRPAPIPSSAPRGPTEPVLRRPSSAEKPLEPGPSSSPSSGRARGAMASPSSSSEATGKPRGRDGSPRMG/VGGRPSRKEEAGAVAGGGKRTARGLRGRGGPAATGQEGDRHPYRWRRQRSGILHEF*AASGFPPPPNHGRHTVQAEPPEPWPALPAAPKPLASPEAGMAGPGGRRTTSLPKRRGCGSCCRGEAHSPTTARTGEDAPRPGREETGTQTGGDRRGAA/RGSP/RSPWA/CIRAPLPSLGVAPG/VPSGRLAHGDILISPCTLPHSELGSPGH*TQANFL*DPGRRRTVLWKVFQGRSRKG*EGRGPGRGHNYDGSVTPGNFIA*SPS/PLPLPPSFTWTLPKTRIPECSGVTKCSGTLGTRVW/RPGSWGLHPGSAPP*LRRPSSAEKPLEPGPSSSPSSGRARGAMASPSSSSEATGKPRGRDGSPRMGEEDVPPE
3433	33801	C	3470	365	589	
3434	33802	A	3471	1	465	MVTTTCYCKKAKPIPRRCSAKEWSCQLPCGQKLLCGQHKCENPCHAGSCQPCPRVSRQKCVCGKKVAERSCASPLWHCDQIKE/CRSQSCS*RRKTKTTG\ELEAFENRLKGRRKKNRKRDEVAVELSLWQKHKYYLISVCGVVVVVFAWYITHDVN

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3435	33803	A	3472	1	444	YSLVEFHTLVLQKSDVEAVF/SKYCFIVGCSVHKGFAFV*YVNERNARAAVGG\MYSSSFDLDHDFQRDYYDRMYSYPAHVPPPPIARAVVPSKCQHVSGN\RRGKSGFNSKRGQRGSSKSGKLKGDDLQAIKKELTQIKQKVDSLLENL
3436	33804	C	3473	190	265	
3437	33805	A	3474	144	316	
3438	33806	A	3475	3	342	
3439	33807	B	3476	180	1370	
3440	33808	A	3477	102	1054	ETLPSNTMASNVTNKTDPRSMNSRVFIGNLNTLVVKKSDVEAIFSKYGKIVGCSVHKGFAFVQYVNERNARG\AVAGEDGRMIA\GQ\VLDINPGLQSPKVN\RGKARCETDLQAEMYGLLF*PWTYDFQRDYYDRMYSYPARVPPPPPIA\RAVVPSKRQRVSGNTSRRGKSGFNSKSGQRGSSKSGKLKGDDLQ\AIKKELTQIKQKVDSL\LENLEKIEKEQSKQAVEMKK**SQKEEQSSQLR*KKDET*C*RLEVLKGGAD\DSA*GRGDLL\DDDDN*RSGGIDQLE\LIK\DDEKEAEE\GEDDRGQRPMGGDDSLST
3441	33809	C	3478	216	350	
3442	33810	A	3479	1	3048	MGLMVLNVENCSSFGWIGRAPPRNTTVDLNSGNIDVPPNMTSWASFHNGVAAGLKIAPASQIDSAWIVYNKPKHAELANEYAGFLVALGLNGYLTKLATFNIHDYLTKGHEMTSIGLLLGVSAAKLGTMDMSITRLLSIRIPALLPPTSTELDVPHNVQV\AAVVG\IGLVYQG\TAHRHTAEGPVGLR*DGLLFLKCNTALTGSHTP*AAGLALGMVCLGEQGPCCGVWEELGERETFKDLIFNRKAPEGSNAT
3443	33811	A	3480	173	422	AAAERGAEEASGGAPPGILEDAGRERRGSGGGR*AGPVGDSKDGVGAV*PPQPHSHRDHHQ*PGPLGGPGCSG*PHLREGLET
3444	33812	C	3481	241	426	

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3445	33813	A	3482	3	826	RGEEAVSGKAGPDSPRAVLRGQGQVWGAAAERGAEEASGGGTQGEGGREVFDS*GTCSLGFPS*PGEQLMGLVYTLGG*PHSHRDHHQ*PGPLGG/HGCSG*PHLRWVPVSALGGRGVGADQLVRVAQGSPETPCSLSGESWPA/GLPGPTPPGWQ**PGP*RAPGLQKAPKGPSYQQGPAPPSHRQSTAQRGVRPRTKRCPSLGCGDLSLLSLAVPVAQPAPRCAYRMLPLLFLLGRLTPVPSPLSSDKVIYNLHLQFIVFTSIKFSATPFKKKKK
3446	33814	A	3483	135	396	LCWLQIHRQGRKPCSPPSLKG**ATCMPPRRRKGGFLSSVSMDIITHSPGNEKIKMPPPTMSKQPGVLQQDCREKLSHCLVCSSLG
3447	33815	A	3484	256	1860	RAPETPRKILGEAGGCRGDGDRPAFQPVRNSRPFLSKLLGQCGRSTLCRLCFRSLNHLFWLFPGPGWRGPGGHSTEDGSLQGKAGQDFSC*NLEISFFP*PSPTCSPTLHCGQKPRAGQGHLHSV\PGAPCWAEVPALLPRRVGD\PGPDILPPSTRV*RCPLDRNSPILL*VHFLKDRATTQNTARPPMGWRPLQQSRQISPAVGGKLCSLPVMI*ASPHPSASVVGETPA*IGGWGW/P*GFQLIG/LPHVRGTQPGLLESRVPSVRGTQPGLPGLPESRVPSVRRTQPGLLESRVPSVRGTQPGLPGLPESRVPSVRRTQPGLPDARVPYVRGTQPGLPGLPESRVPYVRRTQPGLPDARVPYVRGTQPGLPGFRPSRVPRSFCEGDAAGPPRRPRSYVRGTQPGLPAFPSPAFLVRVPSLRGTQPGLPGLPESRVPSVRRTQPGLPDARVPSVRGTQPGLPGLPESRVPSVRGTQPGLPDARVPYVRGTQPGLPGLPESRVPYVRGTQSSLPGLP/GVPRSFREGDVAGP
3448	33816	B	3485	111	258	
3449	33817	A	3486	1	4455	

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3450	33818	A	3487	1	2302	MTECLDRFIDSIAAVPRSTKSTVQKCLPCLSDGEDKIPDLIAITWTPRQGELLEKNVISETGTLLPTPCLDTSTKETADKSTSGKTIHQSIKTVLKDLSGSIDDLPTGTEATLSSAVSASGSTSSQGDQSNPAQSPFSPHASPHLSSIPGGPSPSPVGSPVGSNQSRSGPISPASIPGQDPGYGNS/DKSMGHEYSQR/SFLEDRFPIAVWWPRPLRLKNCLSVLSYSSPSEVTPHPKSESSGTS/SAAQDLQGCSQDVGQPASSSGGSTREQSTSSFIRIVAASSPSSCWKLQVLLSG/AGGDYSPVLLIGGYSRVCLPQ*SDASAATREP/GQNPVPIPP*ASHQCHRKEGPPCRQQAGASQMLSRD*AKQLKPSSSHTLSKHKTT/GTRKSLLFGIKKAYNFTNKYYSELMTQTRPQSTPSIPSPLPLDDAGLERSQGNVSASSFMVLGNRERGEDTTGAGFGRSRNKEEVPCTIYVGAESP/EMC*WMDHT*RKEGKGGLVGVPCV/SREHLEEWQYQLQR*ISLKTQQV*RRKSEVLLGRS/SNTAQACSCWQLTCFMAGTQRNPQMAQYGPQQTGPSMSPHPSPGGQMHAGISSFQQSNSSGTYGPQMSQYGPQDGGGDVSDVVMAIDDDGSCHLLGSAVPGAVLVTFNLLLIIVVTLQMTEPQFREYITGDPLESTCRHASLALAVVLHQETAMTMITDSLAVVPHSG

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3451	33819	A	3488	2	1427	EEPSRREPR/PPGHAPGAVAGGAGPMARAGARGLLGGRRPPGLRL/CARASARVAAG/CGRRRAAREPPRRRVPRRPARQPRRGATAAAATTT*WASGTRPSTAAPEPTASAAAR\RLPLLLPRRAAAPRPEPLFQLRHAGLGPDRPAARPRPRHRSAPGPRPRAQPYGRLRCVRRRSAAGDGG/EPGLAFDEVGDRGPPLTAVPAG\ADRASEAAGPPGATASHPGPTER*QRGRSEPGHRTEPRLTPRSRQEAPQQRAPGVGRPGAPARPAAAGRRDPLSSPELGCSARRHSSLPCPRRGRPAGL\RQRFPALEPSPRQPPARAPR\HPRTCLRRWTPAPGPRRSTRPLPRRAPMPPGPPVARPGP/PPLSHPTARAF/HGTPATRARGPAPVQCEDA*DLQPAAPRPLRQRGPRVPVPKDQ*QDRGHRVKRGRGA/RRGMGWGPVCPSEPQATGRGAPAVRPALLSASTAVVSWSLQAAGSSCK
3452	33820	A	3489	1	262	
3453	33821	A	3490	411	1919	RSYGVRWRRHAPPGRRSSPRIGKVKSASRAWRLRCCGCRRPSRTGMRWQMRWPMVTLARQPFWRRSVSWRGAWGSWRKSWRRSRATRSCSMTATASCSCRLSRIDDISNYEVNLEPGGHDDITSCQGRGRSLPQRAPIGLCCSLGGGAVLADTPLFLPRPKPRDGPGSRAFQKRQQQQSALRVMQRNCAAY\LKLRHWQWWRLFTKVKPLLQVTRQDEVLQARAQELQKVQELQQQSAREVGELQGRVAQLEEERARLAEQLRAEAELCAEAEETRGRLAARKQELELVVSELEARVGEEEECSRQMQTEKKRLQQHIQELEAHLEAEEGARQKLQLEKVTTEAKMKKFEEDLLLLEDQNSKL\ARLGA*GQLGKWGWGALVG**MVNFTPWGLPHCGSQERKLLEDRLAEFSSQAAEEEEKVKSLNKLRLKYEATIADMEDRLRKEEKGRQELEKLKRRLDGESSELQEQMVEQQQRAEELRAQLGRKEEELQAALARRQRFQ

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3454	33822	A	3491	3	266	KMRRLIKSKKDI\NRERQKSLSLTP\TRSDSGEGFLQLPHQDSQDSTSVGTNS*E\DGQTQHPRPI*DAQSSVCCAGSQHGM*ANHSQE
3455	33823	B	3492	1	241	
3456	33824	A	3493	1	1486	SRLHKLCNKPRRSGTTNAKRVGPDCHPMGREGAR*HHALRGRRGEAGTRGGRQRRREQDWREAGPGPRAEVGRTAASARRARGSAPGPRGPSRGRSRWNTGQPRRNRGRGAERPRMQRSRPENGARGTGAGLRGFQPRRHPGFPSRV*GSKDIPAARRRVETCPGPEPRPQPQLPPRPWKGGGDARGDPKFPQAPNAVPGFCVIPAGGVLGAPTAAGLRPTGDVALRRPAGSVEPSGS/AGSQSQCLLCGPVPYRQQTSTGP*PGGWGSP\SDVPCSALISGTGC/PKAQHVSGSLSQRSLSLVDFGRPAS/RGSLFPWPLGTGGKS\PAAPSPQTLWQSS/P/GFLYFPGE/RKGKG*SGPGAGCEP\PIAVGCQEQPRGAEGNLPPKPADPCAGTKQPRAQRGVQQGTSQ*PSTVVMTSGRGAHSRGGPVRRGAHSREVPAAVHGGD/GLLVEGHTAGRVQQPSTGG*PLVEGPPAGEGPFAEGHTAGRSSQLSTVLTTFLP
3457	33825	A	3494	3	393	
3458	33826	A	3495	145	1089	VYRTEFLQDRNYFFLSLVVSAPRTVPGTWTCLLSE*RNE*ILGCDSLFPKAGQAP*VAHITLGFQSSEYSKWKFTNSPTFLELLEEFPSLQVSAGFLLSLLPILKPRFYSISSSQDHTPTAIHLTVAVLMYHTRGLQPARATLMSTHSSSHPEGPLPAAVSGAQCASGFRLPEDPSHPRVLIGPGTGIPPFLSFWQQRLHDSQQKGVAGGFPGVQGGRMTPVFECRSPNEDHIYQEEMLEMARKGVLPAVPTAYSCLPGKPKVCVQDILQQQLASEVLRVLHKEPGHLYVCRAVCMAWDVAHT/L/KQLVAA*LNLN
3459	33827	A	3496	292	478	

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3460	33828	A	3497	87	992	TACGFIACIG*QRLEYCY*DHK GKQQEVLSKHLQMAMDISHIR RNVSCSGRNKASSKAYGTGGS QGRACDLGHNF/TTPSSWERHC TLTSQGVDDFLNAKATFKIFDF SDAFVLSKVGFSGILIQKDENKE ELSDKDIYMEAGIFVSANRGPG VDYCGNRGLSIQGHGGWTLRP SILVSPGVEVRGNEDSVDTAAC IPAAPAPAPTLAERCTGTAWVT ASEGASYRPWLLLHSVKPVSPH STSLETWEPPYIFQKMYENAWC PDRRLPKKQSLMGNLYLGSAE GKYGVGAPTLETTIMQTPDS
3461	33829	A	3498	1	382	TADCAKPVPLAVVSLDSRYGQ WESRSSIHARH*LNSSSSSSSSS SSPPAVYPRFIEFIHFDIQSTGQK SHRVNTRRGP\RDALF*LNSLIP LVRTSSKSAARRRP\GEAPRGTA VPGADPAGGTRPR
3462	33830	A	3499	229	367	
3463	33831	A	3500	233	525	WYFPAGRAGPADPGPGPLAGT PGAGAGGLPTYSTPLRVSSPVP RLESSSTG\SSFPADSAKP\VPL\A VVSLDST/RRDSGNSRSFHSWG VIN*MTRHLVH
3464	33832	A	3501	386	729	TGRGCCLPCTWRIRAQTCLT*T QCC/SCPTTYPGGGERRERERK RRGEKEKQKVLRKYKEAMSNK VCKYFDEGCGSCPFGENCFYKH VYPDGRREKPQRQKVGTSSRY WAQRSNHF
3465	33833	A	3502	63	559	HSSTCECT*DSRCGCKWRSAKQ FESKIIKSCPECRITSNFVIPSEY WVEEKEEKQKLILKYKEAMSN KACRYFDEGRGSCPFGGNCFY KHAYPDGRREEPQRQKVG\TSS RYRAQ\RRNHFWELIEERENSN PFDNDEEE/ALSPFELGE\MLLM LLAAGGDDELTDS
3466	33834	A	3503	374	656	RRVGCRCFHPSQTGTCT*RPPW NVHH*PATCHLAYNRHSWSPH RA/HWHIATAIQLSAHVF/ACHY QQLHHYHQHHHHHHHYRHHH HHHHHHYCHHH

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3467	33835	A	3504	1	1337	MQLQILTIFLDLHHNTNICNELESSNVDDPCDIWEKVHISLIFTAKGSKIPKSSDFQADRELNMFDIISQYDGCPGSIGLTSGAGSTHHRAPWTQTYPQGPTHLSGSPGCILASITGRVTKMPESSESPAWELPRFTELFLSIKDEWTCIFLQLCCPTMLLSGFPPIRIEPWSPLSDQLNPIPLEAAIATHSRIHHCPLVFTASLPGPLTAGNQMADRLVATAVSNARHFHNLTHVNASGLKCRYSNTWKAAKAIIQRRPTCQKRKIK/PDQEQPVQPV*AEGVRFWREDH*P/SHIRSRHSRMTSVSRRQSTWWLPSVTWT/CPTTEALEYGSGACLGCPISGVSKGNKTRSGAAGFH/SPAFKSALCIWRFKQQHANRPYVCWGMEHRSPYSLLPRSSSSSHPQIHGNLDSDDLQVQRGECFICRPCFHRLRSVPDTDTQCPQPR
3468	33836	B	3505	1	1158	
3469	33837	A	3506	35	369	
3470	33838	A	3507	345	564	PCASRTPVSSPWPV*PQPTSARRSPRCLPMVQ*AARASHDSQLCSCRFCVVVTPCAPQGQTCTRQVCARVTHG
3471	33839	A	3508	437	946	SFSSKIVQRMSSSCTENMHMSPSAPSSPQRPGALSLS/RPSGVGGLLKDPIAPC/SR/RLPGILSLSPQNPRAASPDSPAGFWDSVLCTCRLLRVACLCAVRSPRPRLCTRSCKGRGSSMVR*GGGLPIFSSSFSATSLQLSSETVARVTPADECPAESPLPSHGPVSCQGIT
3472	33840	A	3509	1259	1497	KSNMSLLMVFSISSGITVTMCSSWGHLQCRQIFLSLEGLMKTSRSGPWAVL/RGWFSHT*ALDEDAALGHPWASTRKQAPS

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3473	33841	A	3510	268	1278	SPSGPSSSHQPPALKGQVLQCLLSP*ISLRLNLHLWDVYLVEGEQVLMPMACTAFKV*WSKSTCAQWHWAFLLCLFFLLFLLDSKKDNRPPVLRAGAQCMCTAHVEVLPD\PSVFLSAKPRQGSSAARAVLASRGRKALCSG\IHVPTPSGLGCGGPLVP**FQTELLSSCPF*MCPGQPSCPAIPDTLENAVQ\EEAGPVKAMREKGEHGIPAAQPASS\SPGSLVPTCGTVSPSQGTIRRPRGAWPRPQPRLTPLLSAPPWMRHLH/RSLWVGTISQEDQLATCWQANHTVEGAEIGFHCTKPQCGRGFAGPQGLGSATSTWNVLSSLQASRSIWDTAH
3474	33842	A	3511	1	1557	MSRISDDCSELCPLKAIKKERRKEKKQEKWETYRE/REKRQRGQRRRNGERKKRKNTKKR*NAGREGEKKRQKGKTEERKRRGGRRRRETKEEGGS*RNKKQA*SEEKKGRTGKNRKERRKEEGREKERK\REKDRRGGRQKNKTRERDWGGEQQKTEREEEWARKRWKVPGGWEREAPHRELEKNEQLDKHSSSRAKLYDAGQLDLCSNLIQSCDPECPMQATSLTRYPTTTQIFLRGAQGWVCVELFRSYGVEDTSAWERDMRNFGCMTREKQGKPGQLLAHRHLCAHQKMSLLCADNSQKGCLSPANAAPCYGVQVAILTSAPTCPYHLEPLCRSFSLSDQQEAISDPRTAVRIARSGASSNPRLCVTLTFPRVLQPFPHPPQRWGEATKGGRLPAKGSPARTAAGRCGRSAGMPPDARAIFTSAAALPKSRLVPSNIAFKGKRKDLSTKAAAPNLLALRYPRPSAPVGGSHAPSPGQQLQPEEEGNEEEEEEEEGDRAPVFTTGRKDRDSLAE
3475	33843	A	3512	1	525	
3476	33844	A	3513	69	707	LRQNQHEVLKDPRTHTHGGQMGTSSPEQRSTASGAPGWRATSSCVLLASPHHVHHAHGSQEAASTPPVPWTQREYHGWPPGIYPFSSHLHK/RLLPNPAREEL*RRQQAPWKRHCWRDVTTPESTKNLVESSMVNGGLTSQTKENGLSTSQQVPAQRKKLLRAPTLAELDSSESEPRTAVHSSCTAHRCSAWCLAVSAVCPSRPCQSQRGLALS

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3477	33845	A	3514	81	446	TQGGRIKRHLGTSASPTGIMKYPPYCTCPCFQSALHPVPGGLSGKEAESQ*LSPHHPSSQAPGEDPTP/SQP/RLPKHSTLPALGFPATCGR\SPSPKPALPPRGTAPAPPHRYCCYYFPNRSHE
3478	33846	B	3515	58	1034	
3479	33847	C	3516	1	1470	
3480	33848	A	3517	1	606	MAGEDETPVPLPICGTRPI/DAAAAHMAPVPSHLRKHQRVEVHGFCQVQPSYGPGEDRGLADRGSTDEHNPGAAQPRAAALHAHPGGVSQLPAPAH*AGQPPPTEPQLPVSPA*SNPQVSAPSLSPKQLPSPGS*DPAVPGLAE*K*TNSCPRDYTAVAAVLGSAPAAPAQLHPACTLRAPSLRALQEAGAPQPPMGGSGQR
3481	33849	C	3518	76	1275	
3482	33850	A	3519	1	508	MTRQLSNCWVAAECCDPLRHVTQQVLQEAPIVSQAVGGPSRTNLATTPGSHRSTYCLSGAVSSRNLIEPAGEEAGATRARAEEPPGRLRAPSGGVPSPRPLCCRPPVAGCGSGLKMDEDGGGEGGGAVYCNLELKASGVILAVAAEKPSSGQAVLTNTEHSEPSHLKGKSSEKSYLHATPKEDIASFIAFLNVYKQQGPP*APSYSTL/PPPPSPPPSSSILRPLPQPATGGRQQRGRGLGTPPEGARRRPGGSSARARVAPASSP/DGLDEVPRRDSSGETVSRTMAARGCGQVGPAGASYSL
3483	33851	A	3520	451	487	SPLEKSWPGTSHTWFP*SRP*NPGRPLPDPLPADP/LRGVPPPNQRKGMSESSRALITPFHPPLTPAPL*NRPFLWSLF
3484	33852	A	3521	1	758	TPRAPLCRGAASAARS\CKWAPWPSRPRPRHP*SCAEAREGSAAQIPPASKLKHGGPSPPAA/PRRGHPRLLPAPP/VVPLPATAPAAVPSAPGKPFPTPPGLPKADPG/PIGGPLSAFSGSPPFPVH/EPTVLGSPQSTRNLPRPPAA*PPVAWARDAP\GSSPAAAAAKQTFASTQQTPKTT*EPRSPTGPAPALAKLFLTPGTCAPGQPSRKIKLPSRPVAPMGTIENIGYITKAFDWNVLFSDTTKGVRVDCMVQ

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3485	33853	A	3522	3	801	TLLMSHQKLLPLPQIKTPRSFHHSRHLHHQHRHHQKQHHKKHHHHFYYHH*NHHHHHHHCHTPSP\HHHHRHHYYHHHHHHPHQHHQHHNINHHYHHYHHHHQHHQRHHHPSCTVCPQEE*/HNEHRKRPHRCWKVQDPR\NLGYLYIPTTHSELRLALSKHLPSFL*NKVSIYYRQSPDLCPHLNLNPHQYHHRYHHQYYHHHRRHKHYPHHHHHLHHHHHNHHHQNHHHHQETPLHRTLGLPQGPRRRSSAAQPPPPPPPPLLSRRH
3486	33854	A	3523	3	229	WDPPPEFPGRRPRRESSGFPASILLVTEPGARSPPRPAAHS\HPPSPLHRTLGLPPRHPDGAAAPRSSPPPPPPSP
3487	33855	A	3524	1	1257	MKAEIKMFFETNENKDTTYQNLWDTFKAVCRGKCIALNAHKRKQERSKIDTLTSQLKELEEQEQTPSKASRRQEITKIRAELKSWFFEKINKIDKLLARLIKKKREKNQIDAIKNDKGDITSDPTEIQTTIREYYKHLYANKLENLEEMVEFLDTYTLPRLSQEEVESLNRPITGSEIEAIINSLPTKKSPGPDGFTAKFYQ\MLEVLARAIRQEKE/VKGIQLGKEEVQLSLFADDMIVYLENPIISAQNLLKLISNFSKVSGYKINVQKSQAFLYTNNKQTESQIISELPFTIASKRIKYLRIQLTRDVKDLSKENYKPLLNEVKEDTKKWKNIPCSWVGRINIEKMAILPKVIYRFNAIPIELPMTFFTELEKTTLKFIWNQQRARIAKSILSQKNKAGGITLPDFKLYYKATVTKIA

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3488	33856	A	3525	2	2133	WRRIYQANGK*KNK/QKKAGV VILVSDKTDFKPTKIKRDKEGH YIMVKGSIQQEELTVLNIYAPN TGAPRFMKQVLRDLQRDLDPH TTIMGDFNTPLSTLDRSARQKV NKDIQELNSALHQADLINIYRIL HPKSTEYTFISAPHRTYSKIDHI VGRKALLRKYKRTEIITDCLSD HSAIKLELRIKKLTQNSSTTWK LNNLLLNDYWIHNKTKAEIKM CFETSENKDTTYQNLWDTCKA VCREKFIALNAHKRKQERSKID TLTSQLKE/LEKQEQTHSKASRR KSRRNG*IPGHIHPPKTKPGRI* VPE*TNNRV*N*GNN**LTNQK KFRTRRIHSQILPEHSAGSSGQG NQAGERNKGYSIRKRGSQIVPV CR*HDCIFRKPHHLSPKSP*AVK QLQQSLRIQNQRAKITSSPIHQ* QTNREPNHE*TFIHNCFKENKIP RNPTYKGCEGPIQGELQTTAQQ NKRGHKQMEEHSMLMDRKNQ YHENGHSAQGNL*IQCHPHQAT NDFLHRIGKNYFKVHMEPKKSP HCQVNPKPKEQSWRHHAT*LQ TILQGYSNQNSMVLVPKQTYRP MEKNRGLRNNTTHLRPSSL*QT *QKQEMGKGFPI**MVLGKLAS HM*KAETGSLPYTLYKN*FKM D*RLKC*T*NHKNLRRKPRQYH SGHRHEQGLYV*NTKSNGNKS QN*QMGSN*TKELLHSKRNYH
3489	33857	A	3526	1	1896	
3490	33858	B	3527	1	1296	
3491	33859	A	3528	1	1095	
3492	33860	B	3529	1	1413	
3493	33861	A	3530	1	1539	
3494	33862	A	3531	1	1167	
3495	33863	A	3532	1	1575	
3496	33864	B	3533	1	1653	
3497	33865	B	3534	1	1932	
3498	33866	B	3535	1	2451	

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3499	33867	A	3536	1	2502	MTELTGIQQPQIVLFEHKGHKL VQGSSSDAGKVNRIYQHYEAS DKFNYTTGLAWKTAPEQTGKT VRKQQIKLNVKKMESRSKMQE HSSSPPMEQSWRENDFDELREE AFRRSNYSELQEEIQTKGQEVK NFEKTLDEYITRITNTEKCLKEL MELKAKARELREECRSLRSRCD QLEERVSVMEDEMNEMKREG KFREKRIKRNEQSLQEKWDYV KTPNLRLIGVPESDGENGTKLE NTLQDIIQENLPNLVRQANIQIQ EIQRTPQRYSSRRATPRHIIVRFT KVEMKEKMLRAAREKEIQTTIR EYYKHLYANKLENLEEMDKFL DTYTLPRLNQEEVESLNRPITGS EIVAIINSLPTKKSP/GPVGFTAE FCQRK\EGILSISFCEASIILIPKL GRDTTKKENFRPISLMTIDTKIF NKILANQIQQHIKKLIHHDQVG FIPGMQGWFNICKSINVIQHINR TKDKNHMIISIDAEKAFDKIQQL FMLKTLNKLGIDGTYFKIIRAIY DKPTANIILNGQKLEAFPLKTGT RQGCPLSPLLFNIVLEVLAGAIR QEKEIKGVQLGKEEVKLSLFAD DMIVYLENHIVSAQNLLKLISNF SKVSGYKINVQKSLAFLYTNNR QTESQIMSELPFTIASKRIKYLGI QLTRDVKDLFKENYKPLLNEIK EDTNKWKNIPCSWVGRINIVK MAILSKVIYRFNAIPINLPITVFT

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3500	33868	A	3537	1	2197	MNNAKENFLGRFQDGRIGTAP VYSPQHQRRRRRVISALPTEPPL VIPRQTGFGVDLQQTPTDLQLR VLTVRRKTTKQEGHSTKTPSVR YHHQRPKEDKTTKMGRNQSRK AENSKNESASSPPKECSSSPATE QSWMENDFDKYTEVGFRQLVI TNFSELKEDVQTHHKEAKNLE KRLDEWLTRINSIENTLIDLMEL KTMARELRDSCTSFSRQFDQVE ERVSVIEDQMNEMKREEKFRE KKMLEVLPRAIRQEKEIKGIQL GKEEVKLSLFADNMTVYLENPI ISAQNLPKLISNFSKVSGYKINV QKSQAFLYTNNRQTESQIMSEL SFTIASKRIKYLGIQLKRDVKEL FKNYKPLLKEIKEDTNKWKNIP CSWVGRTNIVKMAILPKIIYRFN AIPIKPPMTFFTELEKTTLKFIRN QKRAHIAKTILSKKNKAGGIML PDFKLYYKATVTKTAWYWYQ NRDIDQWYRAEASEIMPHIYNY LIFDKPEKNKQWGKDSLFNKW CWENCLAICGKLKLDPFLTPYT KINSRWIKDLNVRPKAIKILEEN LGNTIQDTGMGKDFMSKTPKA MATKAKIDKWDLIKLKSFCTA KETTIRVNRQPTKWEKIFATYS SDKGLISRIYNELKQIYKKKTN NSINKRAKDMNRHFSKEDIYAA KRHMKKCSSSLAIREMQIKTTM RYHLTPPEVEVVLETL/NH/RSW
3501	33869	A	3538	3	242	NLEEMDKYLDTYTLPRLNQEEF ESLNRPITGSEIEAIINSLPTKKSS GPDGFTAKFYQSIVLEVLARAI RQEKEIKGIQLGKEEVKLSLFA DDMIVYLENPIISAQNLLKLLSN FSKVSGYKINVQKSQAVLYTN NKQTESQIMSEPSFTIASKRIKY LGIQRTRDVKDLFKENYKPLLN KIKEDTNKWKNTPCSWIGRINI MKMAIVPKVIYRFNAIPIKLPM TFFTELEKTTLKFIWNQKRARIA KSILSQKN

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3502	33870	A	3539	281	3228	KPRLENYMKNAEASRADAINWKKGY/LVMEDKMNEMKREGKFREKRIKRNKQSLQEIWDYVKRPNLRLISVPESDRENGTKLENTLQDIIQENFPNLARQANIQIQEIQRTPQRYSSRRATPRHIIVRFSKVEMKEKMLRAAREKEIQTNIREYYKHRYANKLENLEEMDKFLNIYTLRRLNQEEVESLNRPIRGSEIVAIINSLPTKKSPGPDGFTAEYYQRYKEELVPFLLKLFQSIEKEGILPNSFYEASII
3503	33871	B	3540	295	2804	
3504	33872	A	3541	83	480	
3505	33873	A	3542	159	729	PTIVGVVIKFSVCISSPWSHLKPTFHATSWLADGDTDGCVLYFASSCSSYQ*HP\CSSVPEPRYGRRIGSEFSAGSIVRFECNPGYLLQGSTALHCQSVPNALAQWNDTIPSCVAPELREECRSLRSRCDQLEEMVSVMEDEMNEMKREGKFREKRIKRNEQSLQEIWDYVKRLNLRLIVVPERDRDNGTK
3506	33874	A	3543	1	1116	MMARGAGVLIRKIYPLNYKHSAVEQVSRAYSFYTQRPVVPEPRYGRRIGSEFSAGSIVRFECNPGYLLQGSTALHCQSVPNALAQWNDTIPSCVVPCSGNFTQRRGTILSPGYPEPYGNNLNCIWKIIVTEGSGIQIQVISFATEQNWDSLEIHDGGDVTAPRLGSFSGLTPH/WKLSRCMAC/DPSERGLSCTWALVI/HKMEPEQPVCGKQHPEDSQGR/KGPGPGPQNHLLLPGF*VSDGRGRSRSELTPAGSFQWQHSPRNGV*LHQPSPAQVPQRLFKWRLLCPQFP\GDFVKYQCHPGYTLVGTDILTCKLSSQLQFEGSLPTCEATPSSQCVWVSPHRPEARLPAHGPAPKRHVCQKASLLICGKEGMQL
3507	33875	A	3544	373	1051	RHLLGAQCLSRAPWCWNNQASFPFPRCPRAKGQGTARASFSWLGCRIQHEGPIRVQGRRRPHRREPAWAHLHPPMPCRQPNLRP/PGSLRVWPC*KSLC*PSPRPARTHPPGQRCHPYRVPSPPSPSPRPPS*FSRTFQPPGGPRTLTSGPRTQETLSPENVPGPGAP/PAPRHRSSGPKADVALRMRGLSRAPPSAARKERGSPESERPLNLSDGSGCCKHFTTVRA

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3508	33876	A	3545	1	411	RGREARNAAAVGAAQACT*FHRTQGPSRLGGVRGQLALPLRAGLGDCIFPV*AKSEFS/HSPLHAPASLCWGP/PPHPVL/WATHRRQDCGTLILQGSPAVSN*DSAPPALACRLSCGGGQGERTAPPSRCGEKTPWEVPG
3509	33877	A	3546	107	550	TFQMNSLTECCPSLRGWGAPQSLPMPALQTPGSAHLRCQGLLSVETEVLWCHPTVIQSAVALKLH*AISPCF*LPPNYPLSGSSL\PTPHACLSLPNLQCASPL*QPPPCPREVAPLSLEIPESFVYGILGTHITGCLCISLVLPLSP
3510	33878	A	3547	54	825	VGGCLAGPQDPDGVFQTSLRKGVNRAQQQRRQLLPGPTPSKAKDSHP*EGG*GASPNAALLSGAGELPRACQCRLSRHLALPTCAARVC*NPVKPRKGRSEPRSGWASQLPGGDSRLPLRPGTSQGVFSPHRLG/EGGKLVLGVLSLSLKQRGFPGE\WGAAVLSPVRGPRTGWGE\DLPRALPDQSDGSGRMRKSAAEAETGPGARSAAGRSDSDSGGRPDSCQTVPAAR/SPPCLRRQKLPRERLPRAPNP*GPRPLGR
3511	33879	A	3548	1	1335	
3512	33880	A	3549	1	903	MPAGYHVLSDVVSVETPGCPAEFLNIRIPPGDPVFDPDQRGDVPEPPRRVPPPAARRPIPSTTQGLRSVGARCGTGKQLHLQPQCEIHWVKPAGLLSLVGTWRTFMSSSELVNIPIGTRYLAQAVTLTVKVCSFTAEASETTSPPGGTNNSRRAALRAVTLTAKVCSFTPEPARPRTHQKEETPNTSEHQKEQTPDTSAFKNCNTHGEGLQLHSLSPGRPPTPPGRPNNWRNPGLKSWNTYPGKVRNFHWLFSKKEIEDIRNTTLRDVLVAVINIDPSALQPNVFVWHKGGFLP\CPQFFP

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3513	33881	A	3550	1	797	ATRFGGNLVLVGLGFEMTTVPILHAAIREVDIKGVFRYCNTTVTLTAKVYSFTPEARETTNPPGGTNNCRNAGLRAVTLTAKVRSFTAEPARPRTHQKEETPNTSEHQNEQTPDTPPLGTVTLNARVRSFIVEVNSQNPLLMWAAPDPAPGQNGPRGLYAFGAERGNREPFLQALGLVLVRLH\NLWGQRLARQDP\DWE\DEELFQQP\RQRVIATYQITSPHTCTYSRTRCFPVKEIDKEQSLTSHHYLSCSHCFGHEQSDHP
3514	33882	A	3551	23	3990	HGHFWLGHGPLWLSAPSWTLILENTTGSRGGIVWGTRCPRKRAKSSTSPVQSLELRTPFRGRCSDLMGGTTTSWSTDG/CSKGYHVLSDLVSVETPGCPAEFLNIRIPPGDPMFDPDQRGDVVLPFQRSRWDPETGRSPSNPRDPANQVTGWLDGSAIYGSSHSWSDALRSFSGGQLASGPDPAFPRDSQNPLLITGPGGCTQRGNREPFLQALGLLWFRYHNLWAQRLARQHPDWEDEELFQHARKRVIATYQV
3515	33883	A	3552	2	663	VLLDERSAALDGAKRDGTLALAAGALCREARAAQVFFLKGGYEAFSASCPELCSKQ/INVSANCPNHFEGHYQYKSILCGMTTHKADISSWFNEAIDFIDSIKNAGGRVFVHCQAGISRSATICLAYLMRTNRVKLDEAFEFVKQRRSIISPNFSFMGQLLQLESQVLAPHCSAEAGSPAMAVLDRGTSTTTVFNFPVSIPDHSTNSALSYLQSLITTSSHC
3516	33884	A	3553	3	669	GYEAFSASCPELCSKQSTPMGLSLPLSTSVPDSAESGCSSCSTPLYDQVSRCPCHREEVRTGKGMEE*CQGGI*KVTCSIIYNGGDTGI*FIPQLSGLTEPSLQL*ALRK*TCWSCPGKWA*FPIYLSSSNRTEFTRYLKLTFPAESFCGYGHWPWL*ASLMNVGYFWISG\GPVEILPFLYLGSAYHASRKDMLDALGITALINVSANCP\NHFEGHYQYKS

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3517	33885	A	3554	3	1377	WAVCATRVGGAVGGTAKKPR SPEPRVTLLSQSKSGFWFGAER PGGLAFPRKAPPCPWPREQTKS TAGPITLGALRPAMVMEVGTL DAGGLRALLGERAAQCLLLDC RSFFAFNAGHIAGSVNVRFSTIV RRRAKGAMGLEHIVPNAELRG RLLAGAYHAVVLLDERSAG\LD GAKRDGTLALAAGRA/LCREA RAAQALLPSKGGYEA\FSASCP EL\CSKK\STPMGLS\LSLSTSVP D\SAESG/CASSCSTP\LYD\QGG PVEILPFLYLGSAYHA\SRKDML \DA\LGITALDPNVLSQIVPNHFE G\HF\QYKSIPVE\DNPKADISSW \FNE\AIDFIDSIKNAGRRVFVHC QAGISRSAT\ICLAYLMRTNRVK LDEA\FEFVK\QRRSI/LSLPNFSF HGASLLQFESQ\VL\APHC\SGR GWGAPANAGLDRGTSTTTVFN FPVSIPVHSTNSALSYLQSPITTS
3518	33886	A	3555	450	719	
3519	33887	A	3556	63	332	
3520	33888	A	3557	573	1309	WCKGEGEATEKGPRAEAQASP LSEEAGAGRCPGCPYRDAQPLL GSGHTLKRAIQDICYGPGHYQA RAAREVHPPGRKIGKQSLRRPC KLETDDHLSRSLRELD/SW*FGR KCAGAGLTERTQGRLRRKRTL SSEGALPQVLELSAEASKRGSL GKPRKFGKKNPGHGAPQPVVF QSRQCLQRILGEHPRTRPCLRN DNPGASSAPAQATFISPSEDFSS SSQARSPALSLSFREGLVMTHG

SEQ ID NO:	SEQ ID NO: of peptide sequence	Met hod	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
3521	33889	A	3558	1	1797	KDSAGPGPPVALLLPGAA/CLSPAPGCRRAAPRWSSPGPRTAAG*RRMWCASASLA*SPCRPPRSRWWRDAGSGWTPHCPASAAWGAEQEPVRSWGPRASQSHCPGGLRAPPPGSVRCSTQ*DCSSVRPAWSRS*GAC*QV*PRCPCRTPATGWAPPPQGRCGPTTAPGSTGPAGRASLCCPRRAHLPG*WPQKLICAHPGAKSLGLACQPHRG\KGTPIEG/PACGT*GGRRGSGCPGRPHTRRRC*PPAPCGRRSAGSAHPARPWPHGPGGQQRDPGPAYRGGQGGRSPASPSGRRLPASRAGRSRAARGTPGRPEPRSPQRRTGTVQPARCPWPPHRAAAGPPRRGSGAPAPLGRTRSFGTAGKAHPWPRRRPGHW*SAAAAPATGVPACRAGSWVSAAPPAEGRPARARRHPGRCPEASGPRGRRSAAHGHGARAGSPQPGAPPCHLPGIPARQPLGLPRRTRCFGGIAQRGRAARHCLLSRPSAKAKRNSSYREPGMGGWRSPQALGEYGKGSQAGSARLSGAASQGRRARHLRGKAPAWNPAPPPSPPPPALGLPLRTQREATRKPRREEARRPRPRPLRPGGANGSPGPPRAARA
3522	33890	A	3559	1443	1871	PFVYTSSLGRPPSIS*QPFVSGSGCSCP*RSRPSGAWRA/RSASSPAPPP/KAP/SPRPGPRATAGASRRTAGPALCGRPR*GSRGRHLFSRPGGTRRRRRAAR/SAGLPAPGGSEPPKSGSGFPSSPYASSSGLIPGNRSPAAAGEL
3523	33891	A	3560	62	864	ALAESRGDLEAGPSSNTWEFWELAGFSVLFLGNRRAALGLCELPSLRAGVEFTAVQRLWSSAGATWWSKLAVPLAGSAGRENPGSLLDGLLFTLENNLSRGQGAPSTPPAARRAAR*DGGQSASSS\PALESPPERHRRLALVSEQKPQEPA/RSSRRSCGTRLPRLVFCSKVCRRAEPGGSVTRREGGAEREAEERKRGR*GEARR/RQGGRKSTRRKKQAIKGKRESQKRRGGRQGRGRAASPPL*EPRARQPRGSAAPSLLRGLSGCL

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
3524	33892	A	3561	3	2701	TGLWCRCPRSARRSVGRRPGTAPAARPPRPAAQKQALGSRERVGTGPGRILRPGGWGCFP\GPRGTEDADQRAARGPVGAGTQQHGRAVPR\GPQNEPDETLLP/GGPSPRGGELRGRSGARGLP*SLTGPAPGPQRGG\G*SPSPGRASSKAGPWKRPGASRASLQRASSM/PASQVDWGG/PGGSPRCNRCRERKPGTGPGWPPRLRSPGNLRPGVGGLGLALPARTAAAAPRPRERWRSPGAPCLGAQ*PSL
3525	33893	A	3562	2	905	HEGFFFFILGCPFPNFIPPNLVSVRKLGVKPAWGAA/RPRLPLAPMPSREGAARSREMRRPRGIRRSPKEGLFHPEGSQGKSQNGADPQRM*REPGSSKSSEPLPRLLGVHQTA*RWETGETGPAIGGPAELDAVHVGL*CNRGFPSSKQRARRRARVWPGPKKRPPARAARMARLASDQRDFSVSRKAGDGRFPVIGIRSGGGAATGSSSRLSVSSSAVLRKPGRTTGAVPAGGSARKGPSLAPMLGPGSVRSASSPSPGHNPGAGS*ERAGLGERPRQKPLAVPAAAIDFPQSPASRSNI
3526	33894	B	3563	149	283	
3527	33895	A	3564	269	452	AGILFLSSSQ*SNARRPTHGALLGDWGPRCSPSPYANRSPSSSLARQCRTRGSTRDLRVRT

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3528	33896	A	3565	1	1877	MDPQLERQMETTQNLVDSYAA IVNKTVWDLMVGVTPKTIMHV MINNRHAPPHGSRGLLWHWGC RWPCWPGGDAGQPYGTSILIEK KREKNQIDTIKNDKGDITTNPTE IQTTIREYYKHLYANKVENLKE IDKFLDTYTLPRLNQEEVESLN RSITGSKIEAIVNSLPTKKSPGPE GFTVEFYQRYKEELVLFLLKLF QSIEKEGILPKSFYKASIILIPKPG RDTTKKENFRPISLMNIDAKILN KILANQIQQHIKKLIHHDRVGFI PGMQGWFNTRKSINVIQHRNR TKDKNHMIISIDAEKAFDKIQQP FMLKTLHKLGIDGTYLKIIRAIY DKPTANIMLNEQKLEAFPLKTG TRQGCPLSPLLFNIVLEVLARAI RQEKKIKGSLQRVLSFLTTQRG LRRSLQPSIPFSFIILVRAMFLLS GLVAVTLGSPSAGNQSTVLSSW SLVAQQEKAVPTLPLQSARPPH GSAVQAAVWPDTLYQSCCPLA ENQTHFWMTGKCVLCWLCSL WSSGEGKGQAISRVLFGGVKRP YPFQGTLFLESPWNLAGSCPVK PALATRGQG*SSAYSTEPVIVQ RNAT*LKGKARVQLGAKKESG
3529	33897	A	3566	770	949	IRYVLCGGALR\MELLTKQG*SS AYSTEPVIVPRNAT*LKGKARV QLGAKKMMSQSVTPD
3530	33898	B	3567	507	1436	
3531	33899	A	3568	43	421	TSAHPGGEAVPS/LTTSTTWSRS SSLVTFTLMPPRGCSTGPPVTSP LCRMPRTTTMPASPVGSSIGQT STTLPSCPQRQT*PSACTGSG*A SAVRCAPKSSSSPATSSSMTTTT PGRATTTTTQTRC
3532	33900	A	3569	210	610	TRKSRRNG*IPRHIHSPKTKPGR S*ISE*ANNR\TEIVAIINSLPTKK SPGPDGFTAEFYQ\STRRS*TTT MPASPVGSSIGQTSTTLPSLAPR QT*PSACTGSGNHKSLTVKSFS QGCAGLPASLTGPLWWRC

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3533	33901	A	3570	1	718	MENAGEREDPTVGNEGEVRLAGPVLRTQDELSWEEDEANPTSYPKGADSYCHSDCQTIMDFSNFNAFSTPNTFALMNTYSCPQHPNSKQFQLPTFVKMGEAVSVFFIGLPHATPIVEHQNDLIAGSVRMQNQPKGSTLQCIILMPQRPPGQTLEDMDYYYSCFSDEKNLGTKKLSSFPWSHSKEVKATFKGRYPGSHALNRHTTLPGTAWILLLGGELAFLTVKDGSPLALPSRPADGMRGRNKARVLSSLNLTASWG*QAQSSELRTSSPGKRMKQTQLLIQKEQILIVTRIARP*WIFPTSMHFLPQTHLLS*THTA/VPQHPNSKQFQLPTFVKMGEAVSVFFIGLPHATPIVEHQNDLIAGSVRMQNQPKGSTLQCIILMPQRPPGQTLEDMDYYYSCFSDEKNLGTKKLSSFPWSHSKEVKATFKGRYPGS\QPLTATPHYLALPGFSF*VGNLHSSQ*RMEALWPCPPAQLMG
3534	33902	A	3571	719	1643	IQKRACSVSARRGLRTGRCGCTAGTTTMPASPVGSSIGQTSTTLPSCPQRQT*PSACTGSG*ASAVRCAPKSSSSPATSSSMTTTTPGRATTTTTQTRCASTPPSPSTPGAATAAGGPLVQGHGRHRVRVQSESHEGHPHGMRPQPHCSTSSTGMSAGPRVPGQV\ASSRMLTHTNGLRGPGGFKLPSHGVLDLQNGTGMPGGAVCCSTVRGPATGPAQTGQRREPRPTRCPWSSVPPLRRGKKDLARRQVESKPVWPGPWEGTPWSLLLGCNLPALSLCCIGTSADRSFRKFYFFQTRIPLLLTDVL
3535	33903	A	3572	1	933	MPEPPP\PPWAPARPKPPRRAPPPAPRRPVPSTTQGLRSAGT/PARDWQAAPPAALSSPEPHFNLIASVQTVMCPVGAPAGMQGSG\PKPSGCRLVLWTPG**KGSIWGTAASMTRRRWTMRSRTAMSPGPQRVPSAPKPSSAPCA*MEGKRSLLPA/TVPGCKKRYKVTWVAVGGPDPTREASLCQPSLLGTDQDLQSSPFHWHLRIRQKMRYRTPRPHAEQGMGEGSHCLMSEHHFEKTQRQFSPDYYPNPSSQLNVNGIKYHAKNGHRTQIRVRKPFKCRCGKSYKTAQGLRHHTINFHPPVSAEIIRKMQQ

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
3536	33904	A	3573	2	316	CLSLPTPPWTPVRPEPPRRAPPPALRRPVPSTTQGLKSAGARRGTGRQ/PPPAAPDCVAQ\SSTVHLAARATK*PSAHSVVSSSPMGVLFLHGLDFPRMTRSQGLR
3537	33905	A	3574	3	1078	SLPPPPWAPVRPQPPL*VPPPAPRCPVPSTTQGLRSAGA/PARDWQAAPPAAQVFTLLKNIKMLPCLEKPGKFGSLVIMREFNNHMWQVELKMPVPSDLPKGTGKTLILPECIQAPCMKSNNA\PSSSSAPSPWML*A*AWLCRYCRASCGISSIPTASPVTMACC*RYMRWGILPISEPP\QTGFSPAGANQRGPLAATLSGPGGEGQSAVARLTGEKKNHPGAQYANRLSPRVGRFINAAGTTGFPTGKRAGHKKEPIPQSFITRAARRSR*PSKASELGRKQRRPV/PVR*LLRSAQEEISAVGKTPGFCQGGNTGYQSQR\RKK*PANRPVKRLP*GGI*SLPGSKTYAVSVRCPDQKI
3538	33906	A	3575	2	969	VSTWETPQYRRPPSPS*RGSREQPCSFSSPRDTPGENHWLSLPQRD*AGPPVRRALGAS*PHATRRPNRGGAS*PDLQPNHTRPFRPFPSKNPCFRFPEPLRAPTLVPGPCKPHSPAASGRVPPTHPGRGLGKSEG/SKEKPMRRTAAPTPIRFPKITGT/PSTQTAADHALLGMRDQSLSGQSPGPKSPDADDQLQNRDHTETEQRISSGRSSALAPESQLQQGCAGIHFRGRFCKAPPLVCERLRGW\PRGKRKGVCESAAQASPMSAAPCSTVPSPINHPRAEECGRTARDWQAAPLAALVRDPLDEASWAPESGGDVENLYV
3539	33907	C	3576	1	444	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
3540	33908	A	3577	227	2141	FCPVATSASVTPVQTRCATRPTTAPSADCVSPRAAGGLPSGHCFRSEP*GKNWAPCPQPALTPSS/PSQTSDSEEHPSSENIPPGYEVVSLLEALNGPLTPSPAVPPLHVL/ERWPPLRNAPFIWQ*WPPAPRQDDLAS*PPV*/PAAVRDSNSKRVSPNPLPKTLPCCMKRKMSIPAAS/TETQLSQRPSVQHLGEECGVTPESENLTLSSSGAIDQSSCTGTPLSSTI\PPQKALPAAAWPSLSCPWHPPRSALTPSPPCLAPTSPLALKRRERLSLPPSLPAGPPQKK/REGLPAESPDSNFAGLPAGEQDAEAALSSHYQPISHASKGDCKSGMEQQGVCEREWGPATVQSDTPAAAVGLAAPGRQAVEGLSVCSLRPPCSSRCDGSGCSGQPTTVINISLRRPTSPRTREDSEKPGQYPKGHTEARQMPGQKDKVAKRSRKV*EEKENGKGPIRRQ*KQAAPRQLGQAGLTHSLKARV/RGGTGG/AAGVLG/GAWAWRAPHQW/PGLIALPARGNEGLSTRASGCGGCTGSPSSASPPALRSISRRALAAFPRGRARDLQPAMPEPPTPSVGSCAAPASPMSAAPCSTA/LQSHRPPKG*GVRAHGAGLAGSSTCSPSAGSTG*S*LGS*VWWGRGEPLCPAQGL
3541	33909	A	3578	26	1141	VLQLLRWRVWSLFFLMFRCVRSFFLLTQKPSWLHPVDPAPGLQVELPASPAPCARTPQPLGGRWDWAPWSRGRRSSGRLGLHRNLRRPGAQAWRAAGPGPCPAGRQLRPGEKSSAAPVGWHCWGTEYTFPSSRWPGC*APHCPGLAGPAG\SPSAGPAKPTPTWNSSWPASAARSPGSYS/PPLPPY\PLQAEGAGSGLGQPRKGLLHL*DVPAEPVLAGPLASGSIPLAAPPAGRGLLAPGPCPGLDLRLL*QLPPPSVFPTTPKTELVLGTPGHGQPHRGGHESSDSAGG/APTPRALRSGWDPSPPSSVCATPTSSGLSSTPQLPLHQRTSSSTASWSPGWGMGSC*VLVTSGAATVGC*RLPSISTS*SPI
3542	33910	B	3579	1	1234	
3543	33911	A	3580	443	865	

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3544	33912	A	3581	2	1524	CLSLPSPPRPPHPWAPVQPEPPRRAPPPAPRCPVPST/TPGAEERGRTARDWQAAPPAAPKEETPNASEYQKEQTPDTPPLRTVTLTVTVHGFILEVSETKNPPIPDTGLQVVPKPLPRHTRGRVASSSIHHIRFPVSPSARAG/APPGHTPCQGTWQIQSSPAQGGGAPN\PLYSAGSALVSSLVLVLQFVDPFVRS\PEHSVIARPSPARPGTWELGRRRTRPSQDPPRGPSGGPWPGRGRGPWRSKTDAAPGKA\ARSPAPGASCELARRGASPGREGLAVGRAAGRGVASG/APSPAEGP\QAALGAPPGTHRSSSPSAQVPSSGARTESPW*P*LLASAGRPRPQPGYHAQEWRKRPRRPVRTRRRFPTKAPARSAGSFETSTFSAHDPGSRGHPWGPKPLPAGGDRTAPPGAQGRGSA\SKAPARIHEPALRGHSGSRGGTPG\GSSALLCAKNCAPGDPGTAGVGR*SGTQLPPRAPLEPLSAPRRVRPVGSGRRREKVPRPGRPR
3545	33913	A	3582	1	3339	MSVRKDVEKLEPSDIVCGNVQCYSCMETNLTVSQKVKHEVTVGPREGATKPNRMKGKEGRSGSLLGEGDFFKDESVMSSQGSSKDGEKRRGKAQRWKWPMQGICRQLGVAKSMEGYQSRRDQGGRGVSDKWPQVCAKKPEFYPTAQVWANFSVTSCQSVTITQLCHGLRRLEISPARSNAMHLNPDPPGQKQNLSPKVNDIITDIESSSGSGAGKFQVISKSDISEVLLQQMDAGHSSKDDPNEYGGWKSPRPRC
3546	33914	B	3583	1	503	
3547	33915	A	3584	1	787	MIKWVSYQGCRDGLTYGWSCSVETVRWLPEVHAADTSCLKISACLSSFSSSYKAPSVVAQAAPPSSPHKTSSLCTTSAP\SRPSMRTTSAPP*\SSAARPSI*NISS/SPESSAATI*N*NMSSSPGLQLHDTQTRTSAPPRVLNSAT/SQTTTSAPPRARTPVPPGSPAPRPSQKNSHTGSFVVFSSTT*DISGSTGSSHGPPAQRLS*T*KAAPAPPQGSISTT\PDLNSGSTTS/SSRSSAPRPSLNNPFS*NSAVKKSAAEVNE

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3548	33916	A	3585	746	2018	THPQERGTWGNRQLFAVLPLPFYTSLETMSMGCGAVVAGQYQKCPFFTIPSANFPWQKQEGMSGNPPRVRRHISLSRSCLTLAVPMTIRRSWEGAPFVGAQDGCRPLLPGRRALLLHLGLAPLL/GPPPPPVSPPWPPCKATWVSAGGRCLY/GCPSAPAPR\APPEFPAPPGFPAPPAASSPSTRCSRGT*SCGPGRPGPLGPAWSA\GQRGQLAVPEPLQAVLGALGLLRPLGERR/PAQAGTFSPTAPGRGAPGASA*GGRISGHSSGDIPRRGPSRGHPPLLAQGSDAIRSTLH/ERLSTRTRPSFKIKTPSPHQRPQQPHASWTPSSGTLSKPSTPCSSSSCAPRSGDGGG/EGHAGLPSQPAAGSQPAAPCQRPEAWAGGRGNRPGKPGAPQGPCFSLPRPQRSR*LPPPARQKPPFFTLLSLFSF
3549	33917	A	3586	1	1911	TIYAVNLFPILPQGDL*PFTMVTMHWGEGNGQIFRGLLDTGSELMLIPGDPKCHCGPPVKVGAYESQVINGVLAQVQLTVVPEGPQTHPVVISPVLECIIGIDILGSWQNPHVGSLTGKVRATMVEKAKWKPLEQPLPRKIVSQQQYRIRGEIAEISAKIKDLKYAGVVIPTTSPFKSPIWPVQKTDGSTKIPGTSTSVKFLGVQ*CGTCQDIPSKVKDKLLHLAPPTIKKEAQRLVGLFGFWSQHIPHLGELLRPIYRVTRKAASFEWGPEHEKALQQVQAALQAALPLGPYDPA/DQATVQLKLPVINWVL\SDPSSHKVVMHKLREEVGQMTMVFTPATLSSLPQHAMMVSWGVSYDQLTEEEKTRAWLTDRSARYAGTTRKWWTP/HQSLSPATPVI/SQWA/HGHGGRGGGYAWAQQHGLALINADLATASAECPICQQQRPKMSTRYGTIP\GKVLQKAVCDLNQHPIYGTLS/PIARIHRSRNQGVEVEVAALTITPSDPLAKFLLPVPTTLRSTGLEVLVPEGGKLPPGDTTTIPLNRKSRLPPGHFGPLLPLSQQAKKGVYPPKKKSLYQKHALSYMSLFTAVPFTIAKTWNQPRFPSMVNWIENMWYIYTMEHYTAIKMSEIESFAAIWMQLEAI
3550	33918	C	3587	44	310	

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3551	33919	C	3588	20	328	
3552	33920	C	3589	288	542	
3553	33921	A	3590	332	528	
3554	33922	A	3591	3	1717	NVCQSHRIPEHCYDSLNVCSS* GIPEYSCCDLNICPSHWTPEHCY EGLNDCPSSNIPEHCCWGLNDC SSRSIPQHCFWGLHVCPLHRIPE HCSWVLSVSPSQRILEHCDENL NVCL*HRIPEHSRCCLNVCPSHR IPEHCCL/ESESLSLTQDSRTLLR L*GSECLSET*NSIILPPLFECLSH T*YSKTLHLGSECLSLT*DSRTS LLWSECSSYD/VENTTA/EGLSI CPSHRVPEHCYEGLNDCPSRRIP EHYRWGKNVFLSQRIPEHCYE GLHVRFSRGIPEHSCCRLNVCPS HRIPEYYYECLNICPSKRIPEYC CLVPSVYSSHRIPEHCY*VLNVS PSQRIPEHSCGGLNFCPSHWIPE HRYEGLNVCLSHRIPEHCYEGL YDCPSHRIPEHSCCGLKVCPSHS IQEYCCWVLSVCPSHRIPEHCY HCLNVCPSHRIPEH*EDSRTLLL LSECPSQRISEHCYEGLNVFPSH RIPEHCYEGLNDSPTHRIPEHCY EFLNDCHSHRIAEHCFSGLNLC LSHRILEHFRWGLHVCPSHGILE HCCWDLSVSHSH/SNSRSL*RVS
3555	33923	A	3592	3	191	
3556	33924	B	3593	58	477	
3557	33925	A	3594	19	367	AIQSWCHHVLQAQPHVELLVP RFIEELGSLVHGH*PRHRLPPAH SHVLHHCQLQLGHTLRPRHCIL QEHACG/RVRCLLQRQAGSPGG WCKRECLFLQE/VKPSVRICTVE MCTISIS
3558	33926	A	3595	55	555	NHFVAEAASCPPRCPFRLDAKK LVRSPSGLRMVPEHRAFGSPFG LEEPQWVPDKECRRCMQCDAK FDFLTRKHHCRRCGKCFCDRCC SQKVPLRRMCFVGPRAAVRGS APWVFPQGGGVFTD\NSSKCS* AEPPSSS/QFGNSEKPETMT/VSS FQ*PEILVSGWRQPL

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3559	33927	A	3596	182	696	PVFWIRNL*SMASRGLRRD*EH LKEAILAHSL/KAKRGGEAAEE ESEASRGWLVRFKGRRCLRNIE VQGETASAAGEAAAGHPGDLA KITGAGGYYTQQIFSVDETTLH WKKMPCRTFTATEEKISAYFKA SKDGLNLLLGVNAPGTYVLRS NISVFLSEEMSSDKRLTEMGY
3560	33928	A	3597	74	2521	RERWAAGPVTCQVTTWPGAAT TRVTWPMTRPATPCAVHGCSC PRSHWSQKCGQPASRAV/SPHP PSTCGSSA/APGPTPKQEAPSAL WPLSGFPN*EPGPGQPGD\VVE KATERMAAMKTEAGVPLVEV QDPVEVPSGR/PAGTCPAQPQH RTPAPCTADP/PALDTPTTTHPA PAPCPTAIAASWPAVW\LPQPG Q*PRCPRLIATCEGQTPAGEEPQ AAATAGEGR/VKASVSPAPRGT PCCGIRWVARPAFSGHRSSPCP GSQGCWA/PSSGVPEASEPRPGE QEPIFRKREFNKEIKSL/PEPAGV PRPAWLLSAP*APSHAELPG*PP PLPCPAKRGQPGCG*APWRPLP RRPSSV/PPPAWSPP/QDLPPLGS EPAKPTNGG/PALCFPPPHSLQP QDASEKTQG/PEEAPPPCLVPR WPPDSNSR*HPRRSPMSPAPHS TPGRRHLTQIPNYKTHLFP*APA RGPSPGRACTSPCPRQGLWWR WPAARATSGALSHLHFPPPTPA LPATFSLSSLQLPLHLPPHCVQR APAAAAGSRRRSRCPPSRRSPA CLTSPTAFMRSSPTS*PSRQPPW SSASTSSKRTSVSSWASSPSPSP TCSGTFPWA*RR*KAPASTCPR RPTGAACCVNWRSPKGPGRPP GSAPPTAAQRHPLCSRNQPPTL PRTRPQSPAAPSTPTCQPAGSSA LWSPSSTCLPAPAWVPVPPSPR
3561	33929	B	3598	1	588	

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3562	33930	A	3599	357	1011	FLPLGELYAEGSRMIWSDGFWAGHLHSCSHPRSSSFSPTCTYPLPPPPPWVERQGTRGSG\P*PGKRTSSPFRVSPGSNTRECTPS\GLLDCIPSCISLSEKPQNDSSSESA*KIPASSLVTSGLGFCKNPQWSNTSCTSLSCDA/CPPWND/CCQMPVPCSWTFQPPEP*AK*TSVPYKLPSLWYSVSQRGKDSPSPAPPGPGRRAQPASRAAAAPPAVGP/SDRAADPLSPLQAPIWAPRHQHGRSPR/VR*GLRWLHGALRVVVILEGGRAQ*PPWNDFVRCQCHALGLSSLQNHEPNKLLFLINYPVCGILCPNAGKTARAPPLRARVGAPSLPAALLLLLLLWDR
3563	33931	A	3600	63	660	KPQVNKSASCAQLAGPVSQRGKDSPSPAPPGPGRR/CPACQPRCCCSSCCGTADRAAAPLSPLQAPIWAPATSMDARRVPVRVFALTEART*GRAPWAFPGDVNPSLAPIP*TCSYTELIPPVSFSFPPSTSGNSPTACLDSGVQLASPSGSRTGATGGAAHSPARAPA/PPQPLGSRWDQGLRWLHGALRVVVILEGGRAQ
3564	33932	A	3601	202	515	FCKHEAAVSSGKAVGTRSQCRHSGPLRVAMKFPARSTRGATNKKAESRQPSENSVTDSNSDSEDESGMNFLEKRALNIKQNKAMLAKLMSELESFPGSFRGR*PRGCSAAPRSKRRSGHPPPAWT/CSPRAAERS/PE*RRT*RNSDM*S*FPARSTRGATNKKAESRQPSENSVTDSNSDSEDESGMNFLEKRALNIKQNKAMLAKLMSELESFPGSFRGRHP
3565	33933	C	3602	40	186	
3566	33934	A	3603	1	3189	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Met hod	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
3567	33935	A	3604	1	1821	MLKNFKKGFNGDYGVTMTPG KLRTLCEIDWPTLEVGWPSEGS LDRSLVSKVWHKVTGKSGHSD QFPYIDTWLPQWVRGQAAAVL VAKGQIVKEGSRSTHRGKSTPE VLFDPTSDDPLQEMAKVIPVVP SPYQGERLPTFESTVLVPPQDK HIPRPPRVDKRGGEASGETPPL AARLRPKTGIQMPLREQRYTGI DEDGHMAERRVFVCQPFTSAD LLNWKNNTPSCTEKPQALIDLL QTIIQTHNPTWADCHQLLMFLF NTDERRRVLQAATKWLGEHAP ADYQNPQEYGKEESPAQFYER LCEAYHMYTPFDPDSPENQRMI NMALVSQSAEDIRRKLQKQAG FAGMNTSQLLEIANQVFVNRD AVSHTGAEHSVVTGPVAPLSK KTIDIIGAMGVSAKQAFCLPRT CTPGTKDYRLVQDLRLVNQAT VTLHPTVPNPYILLGLLPAEDS WFTCLDLKDAFFSIRLAPERQK LFAFQWEDPESGVTTQYTWTW LPQGFKNSPTIFGEALARDLQK FPTRDLGCVLLQYVDDLLLGHP TAVGCAKRTDALLRHLEDCGY KVSKKK\AQICQQQVRYLGFTI RRGV\RLGSERKQVICNLPEPKT
3568	33936	A	3605	1269	2463	GVQEESSDLPTAVDSSRPDIRD QAWASVHWELYVHGSSFINT* GERGAGY/AVITWT/HVVEARS MPQGTSAQKAELIAFIRALELSE ALAKTVRQRCVSCRQHHARQG PAVPPGIQAYGAAPFEDLQVDF TEMPKCGDIRKIVTGDVNTPAI LGVVSSSPPSHIGNNITEDPELQ PILAGLSLSMYLVTVLRNLLIIL AVSSDPHLHTPMCFFLSNLCWA DIGFTLATVPKMIVDMQSHTRV ISYEGCLTRISFLVLFACIEDML LTVMAYDCFVAICRPLHYPVIV NPHLCVFFLLVYFFLSLLDSQL HSWIVLQFTIIKNVEISNFVCDP SQLLKLACSDSVINSIFMYFHST MFGFLPISGILLSYYKIVPSILRIS SSDGKYKAFSTCGSHLAVVC
3569	33937	B	3606	1	1830	
3570	33938	B	3607	1	459	
3571	33939	B	3608	30	440	
3572	33940	A	3609	1	279	
3573	33941	A	3610	2	500	

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3574	33942	A	3611	370	464	GHACGAERDHLQPHSPAHLLLLLLSV*AVW*PRYTVKMATACHQW
3575	33943	B	3612	1	780	
3576	33944	B	3613	1	610	
3577	33945	A	3614	1	1896	
3578	33946	A	3615	2	1418	
3579	33947	A	3616	314	720	GVQEESSDLPTAVDSSRPDIRDQAWASVHWELYVHGSSFINT*GERGAGY/AVITWT/HVVEARSMPQGTSAQKAELIAFIRALELSEALAKTVRQRCVSCRQHHARQGPAVPPGIQAYGAAPFEDLQVDFTEMPKCG
3580	33948	A	3617	1	1029	
3581	33949	A	3618	1199	1758	KTLSFLSDQPLRARSCLPFSGKIRS/RALAKTVRQRCVSCRQHHARQGPAVPPGIQAYGAAAFEDLQVDFTEMPECGGNKYLPVLGRTYSGWVETYPTRAEKAREVTRVLLRDLIPRLELPFRIGSDNGPAFVADLLQKTATVLGITRKLHAASRPQSSGKGIQNNRTGGVYTPCDIESHVILFRSGY
3582	33950	C	3619	499	831	
3583	33951	A	3620	410	1144	LSIQQYLTRP/PLLGFPPAEDSWFTCLDLKDAFFPIRLAPERQKLFAFQWEDPESGWPPCWRALAATALLVQEANKLTLGQKLNIKASRAVVTLMNTKGHHWLTNATLTDYQTLLCENPRITIEVCNTLHPATLLPVSKSPVKPGCVEVLDSIDSSRPDLWDQPWASVDWELYLDGSS/FLQPPRRGGGYA/VGDTSELPPCWVCGIPALTQRLEKQHLPPSGHQGSLKHLIWDLLLLTKKRTFSSMI
3584	33952	A	3621	1244	2690	
3585	33953	B	3622	1	1114	
3586	33954	B	3623	1	1863	

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3587	33955	A	3624	3	2056	REALQGIQVRLKHLRTFGIIVPC QSPCNTLLLPFPKPRTKDYSQV QDLRLLHQATLTFHPTVPNPTT LLGLLPAKDSGFTCLDPKDAFF PIRLAPERQKLFAFQWEDPESG VTTQYTWTGLPQGFKNSPTIFG EAWARDLQKFPSRDLGCVLLQ *VDDLLLGHPTAVGCAKGTDA LHRHLEDCGCKVSKKKAQICR QQALAATALRVQEANKLTLEQ NLNIKASRAVVTLMNTKGHHW LTNARLTQYQTWLCENPRITIE VCNSLHPATLLPVSESPVEPRC VEVLDTIDSSRPDLRGQPWASV DWELYVDGSSFFNPQGERGAG CAVITLDTVVEARSLSQATSAQ KAELIAFIRALELS/EGRKGLSPG RGKDK*WRKDGFGYRMGEYC ATAARSCSCTGCARNHPSTSGV TGKVVRPVFLHLAFVS\FAKTV RQRCVTCRQHDARQGPAVLPGI GAYGAAPFEGLQVDFTEMPKC GGNKYVLVLVCTYSGWVEAYP TLTEKAREVTRVLLRDLIPRFRP PLRIGSDKGPAFLAALLQKTAK MGTRSDTQLAHIGTVLRDIHVS VCSDGPNLRTGLNVILGGVEW QSTPGNLVRRQGETGLHLHIYH WWQAVAIFPVYLGSSLHMKVG GRSFEQEEDTEHIPVSYDREGQ ECDTELKGQEGDELEAGSVVP
3588	33956	A	3625	491	964	RIQLCCRTRGTGAQKKRMKVS SRCTPAPATRGTGAWQPQAQQ APGVRATEAPRL*AHDEVSQPA PAPPSTRHSPRR*PVAGKEHLE AAVDKERHEVAQAVVTHVLEG QLEDVAPAHAAQI/GSPPWAGK RLRTNPAPRPCHPIQTLSRRLGP QNHTLLH
3589	33957	A	3626	131	351	NVGLKGTAGER\GGSGPPS*PPA GRNSGPAGRRPPAARAPTPGSA AR*PAPPGPPRPPAGRGAAAAA GPAGGGA
3590	33958	A	3627	3	428	GEWEAPPLLRHTRPGPA/PAPPA PSGASCAPCGGQTCRPRPLRQA PPSPITTGHARIWLGQPRPRSSS ATPPKELP*GPTE\PHTGELWVA SGSCPSGTKLPEEGSGSNTYFSA VSAGDTQSNIIWNGPPANSNRP AAEGPDC

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3591	33959	A	3628	2	425	YLASAAIFRNMSSVVCLVCFFFTSQICLQTDNAPYTVLSINENLSVLGSMFSNFLRSFLRSTKASAKPFIVTLLRSSFFSVSSSLASSSAMHSCSSSNSSSFFNSSRTTSKSSSTSSSFTPS/SESF/SS*VSSSRFHSYTPW
3592	33960	A	3629	81	594	LPAGFGPCGAWNQNQREKRPQSPGAESAA*SGGGQQRGGRAGAGGHGACASLGSE/PQGREPALGAGGETALPSGSGSGRPPRPQRPRDSGPEALPSAAFWKRRR*ASASAPALTPVPDSVRGAQPGGGGAEPEGKAVRMRGASRPALSQLSGREIGPCPQGRVVAPSGTAC
3593	33961	A	3630	317	778	PMVWSCASAARLPEPGNGALLRTSSPRCSP/CPSAA*LTRLPPT/P/PGDPSAAPSPGQRPAGLAGAGGAERSGAVEVGPREPGRDGAGS*SWI/AGPPGRLEAGSA/GVLRSPVAGWRPGTCAGRP/GKAGDLGPSAPPQAPHPPPPSWSPLSPLASPPTK
3594	33962	B	3631	1	1068	
3595	33963	A	3632	1	730	LALTARSSHPQRATVPKASVVAAASPTKFRHSGAALQWRNLGPVRAQGRRLSTAAPAAPSRRLFPPPPFRGGRGGGWSGSRGRRGAEPGRSHGAGGPGDDGRCGWGEGAGTSTPARPSRGPG*RPEIWTRGGGGSAKSQG/PAGAPGCAGPRGASSFGRQRAPAVLGPG/SSTAVCPLPRRTWNLRAPGGAPSYAQVAAAHQAPPGRPPWSPRGARGSGRSRTFAPSTPAVVAGAASAVAPPRLRPSPPPAPAPAAAATAAERRGREEAPGRGCGSGRAEPPPLGPDGTQVSPLQRSSRVTEFCGGSGGHYARFWHSSPLRVGASRSQS
3596	33964	A	3633	70	792	HGLVLDVRGPLSHAAPYWAPYPAATAAAARTAPLPPRSAIV*/SGPQPDFQELRKTWPSQC/GMARREPLLPITAIPRVVVETTP*GFAKQEPSVAGLRCRGSEAPA*LLHGVHRNVS/ETPGPEMGRPG*GNHRQRPGKQRGIPSSGLPGRCSGSRGPHSSPGQKPHGSTLSGRRGADPRPRRRVYLSTPLLCEKKPHHDTILKRKPGMGDGNNPCPWNAGLYGQATRFAPLPLCPRRRHG

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3597	33965	A	3634	2	339	WPCGWTGRGGCRQ\RGRERRLGSGVRFGDVSFRGRGRGRARASWKPPHQGPGEPKSGTRNRPP*\GGGAPAGIRGPELGTGNMKKLLLSLPIYYHLAGEKGQVAKIVRIPSADV
3598	33966	A	3635	31	438	MVTDVVTRGGELGQRHVPPGESSGLFCGQCGERETRDPSYRG/WSRRFRFRALKNGAHWSPRLAVFGDLGADNPKAVPRLRRDTQQGMYDAVLH/VGNFSNYKARFSMPGDNEGLWYSWDLGPAHIISFSTEVHFFLH
3599	33967	A	3636	1	422	LRRDTQQGMYDAVLHVGDFAYNLDQDNARVGDRFMRLIEPVAASLPYMTCPGNHEERYNFSNYKARFSMPGDNEGLWYSWDMGPAHIISFSTEVYFFLHYGRHLVQRQFRWLESDLQ/QSQ*EPGSPAVDHHYGAPAHVLTK
3600	33968	A	3640	1	319	FRREPPRGAAAAAALPRRNRENKRSKNRPCCEGPRGSARMKELE*PRPLQVLCLLPEMCSPRLADSYSPVSVRPISAPVRFLHRCCPPPFAEFPACRLLQHSRVPL
3601	33969	C	3641	214	363	
3602	33970	A	3642	1	3390	
3603	33971	A	3643	396	766	ERGLGRSEIPRKEVEHFMQLGSAVAGP*LLP\LVGPAGECFHGWLEPLLARIAEDKTVVVSPDIVTIDLNTFEFAKPVQRGRVHSRGNFDWSLTFGWETLPPHEKQRRKDETYPIKQPVGVIGD
3604	33972	A	3644	105	786	VGPEHCAGAARWVTSPPRSWPDAGQSVN*PDLP*REKHPEG/G*KLQGQGAKTAGNAVVWKPLSK/PQGSSALSGGHWDRLPAPDPGKMPNCDRAPPKIASRVSPQACFPRPSPPVPSAGPLRASTPADQARRPARAARPPDALSKRGPCRISAKLHSGGGGGGGCREKAQEEPEGRTARSLTPPLPLAPRPGPAGRRLPPAHTTQPPGRTGCPSPAGRDTSQLPYFLLK
3605	33973	A	3645	313	546	RNKVGSRGRAKQLKFSGQSTRVHRSESREEEEEKEEDEEEEEEEEEYEKEEEKEEEEEEEERDLEFSKGPFLSS*SSQGK/GTRVHRSESREEEEEKEEDEEEEEEEEEEYEKEEEKEEEEEEEERDLEFSKGPF

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3606	33974	A	3646	3	1332	PLGPRRQQSECGAPTLTWPPGS NGLPGQQGASPLSASPGAGAGS GRGPAA\GGSGASCTPSPRGPAS WSRSAAQVPRSSRWRAGSASS* NAGSP/TPPTSQPPRA/PALCAA AGTLAPVEKGVEVPAGRGLSG APS**GKCPLPEAPSGGSAPLS* GGTESGAGAPEPRKATGRPGPR VPGGAGAA/RGLPAPTSGCAAP FPPRPCPGLCVLRARPAGAAHP CPGPGWPG/PGPGAHQTLRAAL REPSPLASPLVSGRPGPRLVFNR VNG/AAGPLHVPILRGDPGDLH SGPRGECPLCVRSLAAGATAA\ DGGPAGEGRPRPVYTMERTAN PRLQNFVPH*PR/PSGGRKQFLA RITS\FPSGCWEGGAATRPTCRQ EKGMAALPTHCAWLGAGHT*K CQHLDFCTFFFPGPGCGDGRCH VQGPNPSDLSPAHCAQGPATSP WGWQGGAPG
3607	33975	A	3647	102	788	GHCGGGTQCSWPAPWCQNLLP PSASPTLSTQRQLWHAWPGAH RNPV*QVPSLDS*ARAQLSVPA QGSLPLC/ASLTASPWCSCSSLA VLLFGK*PFCVNLF*RASLMKS SSRARVLPSLRPVRWPAVG\RG WQGMERGQGAWPWLCGAVCS RA*SVHMTTLPSGPALCGIQRR LQSSTQRRPESLHPLQLGWEAA QAGEGLPHPAVVHLPASPRLQL SQLHQSRPRLPPG
3608	33976	A	3648	114	1309	TNCSCLRDRPLDSSHVPWVEEA QSAHNNKEIVPQKGPWSSKHN QARGPPRSESNTNKAVNCAGRS TKTQTPRGTSGT/TEGNT*VHTR HTKMSTTNTNTSSLDAPPTTQQ MRSTRERGTS\PAPPSSALKNTY TLPLPTS\SNDTTIYQLTVVPGP GPRTGELPRCHARVTPRVSGEE ALPPPPRSPENSNTHLRTPSQTR TPTRARPPL\PETSPQQPWPDPR VGFFLRSSPVWAPSSQQYPWW SPSLSTNMTIPPESS/SLLPTLAY YTSLTSHHGQRMPA/PADHA*A QSTPSAHRHRPQYVQWTTDPPS THGTFEESSGR/YPQTHTVAVK KKTIGTPARDSHSFPTTPTTRM VKSLKTSTGTSTDLSSSRSILKS PTSSIFTSLTIFSIWRDPDSMDLC V

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3609	33977	A	3649	3	1777	NVAGNPARSMAETQSRAGTAG PGPRTKQTPGTWGSGQAGAPA HPPCYIQESRSGFSAPGRARNA\ PGAANPLCMAPGGAEGSGVIQ REVEGRPRSHSAPMLSLWSERP PSCVCLGPDGAADFPRRGRGPR PPLQDSPASPSAPRCSPARCSRL PL*PRPRDKDAPGTGGRPG/PPG TLPDSRLECSASRPCGEGCETL VQFPDRRGPGCGPLQGPGRGNP ARPQPRLTRAAP\GPTAPAALVS SGGAAVPPRRTR*PLLAGAVEV ASPRPGSVQSLVPEHPGPFKELR NIVLSNSPEASYSAPAN*RPPPA EIRRREWQELRGGVLGGGLVFS FPPHSCVGSTGAWGLPTWRGV GSGIQGFFSVPP/SGRETSRGGR TATAPWSSTPDCPSHWREPSAG SLRRG*GRRDAAPGAR*SRAPP TRPGSRASPG\GAGEAGVEGEL LGPRGQVVTG/PGRPTAPGIYRP GGRRKASAAGSRCATGGSRSSC PRRGSRSPGWRWTRWGVP/GR RGTLARPAPGPGCPYRRRPGGA PRGAGGRPSTGCGSRSRQWLA GQLLPRPSMLGALPGLAPLQPP PAPPVPPPPPPPPPPMPLSAALSS
3610	33978	A	3650	3	922	NVAGNPARSMAETQSRAGTAG PGPRTKQTPGTWGSGQAGAPA HPPCYIQESRSGFSAPG\PRETHS GAANPLCMAPGGAEGSGVIQR E\GKAGPDPTARLCSAFGPSGRP PAC/RLGPDGAADFPRRGRGPR PPLQDSPASPSAPRCSPARCSRL PL*PRPRDKDAPGTGGRPGRLG HSLTRAWSAQHPGP/AGEGCET LVQFPDRRGPGCGPLQGPGRGN PARPQPRLTRAAPAPDSAGSSG/ APPEGCCAPAKDEMTPAGRSC GGCLAETRICPVARP*APLEKSF PNVVNPGKKKAQPTLSPSNMT
3611	33979	A	3651	1	542	LPGAGHRRVLDAGGPRGAGLQ PQLPARQVGAVAELHVSGPPG AGLA/GSGSGASGVGLGAAGW GSGPRGVRAEGEGAYSGPGQV FPVQGNVGNADAGTTGVGVPA GWWPPLPTRLQTLSVASPWLCP *AAASARSPPSGLSGE*TLFYTF SFLPPVVIAASPPAGLASEARPC FPRFHSYP

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3612	33980	A	3652	1	3063	MSLEVDRSVETMCSGDEILLPD LPKADVADPLWGPFPVQNCLS LARSDSREQGLVLVMESRNRE VVPPGVSYSKDGAKSLKGDVP ASEVTSKDSTFSQFSPISSAEEC GDDEKIKVDDPLTRRTCNQASG SAPQQDYDKLKAFGGENSSKT GLSPSGNMEKNKVVKREAEAN SINLSVYEPFKVRKAEDKLKEN SDNVLENRVLDGKLSSEKNDT CLPGTAPSKTKSSSKLSSCSSAI MALSAKKAASDSCKEPV
3613	33981	A	3653	1	847	MENKKVASPGWTCWECDRLF MQRDVYISHMRNEHGKQMKK HPCRQCDKSFSLSHSLCWHNRI KHKGIRQGPDSRRTFTKRLMLE KHVQLMHGIKDPDLKE/TDRCH P*GGNRNKRRQPRSPVPSRSWK NQFWSSGLPKEQSLNH*KS*KS MFLRFTSALVRGFTTENLLQFH EHIPQHKSDGSSYQCRECGLCY TSHVSLYMHLFIVHKLKEPQTV FKQNGAGEDNQQENKPSHEDD SPDGTVSDRKCKVCAKTFETEA ASNTHMRIHGMAFIKSKRMSSA EK

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3614	33982	A	3654	854	3009	VNSHSQLLQRE*NT*ESNLQGM *RTSSRRTTNHCSMK*KRIQTN GRTFHAHG*E/RVNIVKMAILPK KIQSDLTSHEISLEEMKKHNQG KEAAQRVLSQIDVAQKKLQDV SMKFRLFQKPANFEQRLQESK MILDEVKMHLPALETKSVEQE VVQSQLNHCVNLYKSLSEVKS EVEMVIKTGRQIVQKKQTENPK ELDERVTALKLHYNELGAKVT ERKQQLEKCLKLSRKMRKEMN VLTEWLAATDMELTKRSAVEG MPSNLDSEVAWGKATQKEIEK QKVHLKSITEVGEALKTVLGKK ETLVEDKLSLLNSNWIAVTSRA EEWLNLLLEYQKHMETFDQNV DHITKWIIQADTLLDESEKKKP QQKEDVLKRLKAELNDIRPKV DSTRDQAANLMANRGDHCRK LVEPQISELNHRFAAISHRIKTG KKPSWRRGVSNLGEMLVEVYL KALMSEDLRKGINQDEFSPTIY YFPITVFGSEGDLLLGKIRWIQG AYCLMIGQDVFMDTRLRVSAC FLKTKMKTVLVVFDQNEDNEG TVKELLQRGDNLQQRITDERKR EEIKIKQQLLQTKHNALKDLRS QRRKKALEISHQWYQYKRQAD DLLKCLDDIEKKLASLPEPRDE RKIKEIDRELQKKKEELNAVRR QAEGLSEDGAAMAVEPTQIQLS KRWREIESKFAQFRRLNFAQIV
3615	33983	A	3655	44	953	GVHNGVEELILVRRMQKSPGP GEMESGSLEKEPLGTQTGPVPS E/EYGIGLSQSISTKHPETSPKDS RIRENDVTADGRTTEDHITADP GTTEDSVTADPGTTEDNVTVDP GTTEGSVTADPATTKDYVSADP GTTKDSVTADPGTTENFVTADP GTTKDSITADPRTTENFVTADP GTTKHSITVDPGTTEDSVTADP GTTKHSITADPGTTEDSVTADP GTTEDETTKHGDTHLL*TTSVT AVKPTRLLTPMGIILISLAATTV TVVLFVGLGFIVKECFLPPLNPS TRVIYHPHVMDYSTP
3616	33984	A	3656	200	542	CSPPSTRPGPGP/SGTAWPGPRG TKRSSPSSSSSSPSTTSTTTSSSSS SSSSSSSSAPPRGFSSTRPSPLRR LLPPSSSSPSSSSSSPSTTSTTTSS SSSSSSASAGGRRAGTRG

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3617	33985	A	3657	132	853	EIDKKHRFLVSISLNSPSK*GEG DTPSRPHRARTGASVVPSPKFPT SLGRSALSRHPHQTTNPTRPLR KAGAAAFNAPRAGPLGTAWPG PRGTKRSSPSSSSSSPSTTSTTTS SSSSSSSSSSSSAPPRGFSSTRPSP LRRLLPPSSSSSSSPRSSSTGDEA AAAAPVA/SRGAGPGA/SAAAA AAAASSSPG/SGAGAGPGTGGG SPGRAASLAGAGAGPAGCSAA PPRRLPRLERLARRRAC
3618	33986	A	3658	222	373	
3619	33987	A	3659	3	513	IPAALSCCCPEWQALV*QILQDS SCCQSPRVPGHSCGKGTTLCVF SREWSLVSGSRC\SDGETSCTGR CCNAFLCYDLRFSWLFCTLDVR RGVA/GQGGRLGLDLGLSAVCI HQVWVMGSRCG*QLLAPGRVS RPRGRERGTHWSCWCRSPWM GSGWEAHSGAACLSGVFVP
3620	33988	A	3660	3	463	
3621	33989	A	3661	263	1020	SGLREPKQLQMLEL*RKMSQLS LEG**SSHNM/V*RL*KKCSDYS YRDYILSWYGNLSRDEGRTLPS ALGR\FWEIARQLHDRLSHVDV VRSCLQGCCEDLYSLISVT*KLP MPDMKNSQDLLCCT/PCLRNSD DEVRFLQTCSRVLVFCLLPSKD VQSLSLRIMLAEILTTKVLKPVV ELLSNPDYINQMLLAQLAYREQ MNEHHKRAYTYGPSYEDFIKLI NSNSDVEFLKQLRSVEGTVEKS GRRCVLVVFNN
3622	33990	A	3662	1	4314	
3623	33991	A	3663	2	492	ISAGVTGTSGLSAEATGIPGLSA GVTGKTGLSAGVTETIGLSAGL SARVTESTGLSAGVTGTIE*SAV VTETTRLSSGVTGTIGPSAEETG ATGLSAEVTGTTGSLAEVTGTT GLSAGVTGTIGSSAAGLSS/AP*I PSIPAFSGLVFILSCSTKFKAKE WLFFV

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3624	33992	A	3664	1	959	AGLSLMGSI*ACHTGLESSLPV WILSAPSFPPHPVTSSPPISFHLC/ KLSLSH/CT*LGTVGALLPASSA THVHQAWPQWPATLMSHWNC YPREGEEIGYLPTSHPTPHYIPV LTTSA/HSAAPSHFGQSQAPIRL PPPPGAPSISLSPLPQNLCKGYE RDPLPSRPPLRAVRSKKQKLGW RLAGPLSKSPDGINLPFLTSPLG CLDLSLPPGPGPTVLFSVSLWH STKLCQHQSLTGLGGQPGQQG SSSPSAVFRGSRDVSGVIAQRQT SQEKELESGL/CVLTSGAPSPSSP HPPYRGTSLFLFYLCILEKGKM VNKRDLCC
3625	33993	A	3665	2	2180	CPQSLIAVEQRKPPPTGSQVLLQ PRAAQGTPLPTATPHGTSGDAQ KHLLQTW*NTWP*KKPGPSPT/ VRRTQDTDQTTAQHPEGAKVQ GHDQFPGGSVHFGCRPAPSPPR RQG/PLAWHGAGADGFPH/GSP FPSSLTRRCTATPSVLKTSPYRK PLLHSCPSN*MYP*PTRPPPSPTS PTQLSLRT/ANVATCPPLWPLPL RRHLSQWVPPNWEPGAASGSS REHGGI\PAMPQPQCSAPSY/PPT EACLQSADGDQALSKHSADTN AS\RPKPRGSWCPPVTDEDAES DRGSGQQQSQRTPAEVLGKPQ VLERFLLPTQTKQEGSHDEETR HVHNCREGSTEKQGRHPLPARP SPASSKRLL/TPGPSPPAAKRLL RQGLLRPAATPCSASGGYLGTR QRALGAGALGGCEPTPATGEES RPCHLR*PLSPSDSSSLCPLGFA K/PHQARNAGLLGASTGMKAT KWAGACRQRTAKTEAWASSW QRVSDTKP/GSTRQKNKDSGSH PQYQAFDLRLTITAGFSAAEAS ELEGSCAAATQISSLQVACHGT SRPHNHVVDDIMNSTAGPPSGV CGELENVMSGKPTQLVSEMLQ VR\PSPSGASFQQSLRMT*VSVN WTPPRPCI*NRP\AAPAETSPAPR TA/STPNASPQGPSARGFVEKW NGSHAARHPRYKPGTQ*PSGA ASTG/SPGTPPSPALPPCRASSLV
3626	33994	A	3666	3	426	
3627	33995	A	3667	3	266	

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3628	33996	A	3668	2	1256	CHCGPP/VKVEAYGSQVLKGVLAQVQLTVGPVGPRTHPVVIFPVPECIIGIDMLSSRQNPHTGSLTGRVWTIMVRKAKWKPLELPLPRKIVNQKQYHIPEGIVEISATIKDLKDAGVVIPTTSPFNSPIWPVQKTDGSWRMTVGYCKLNQVVTPIAAAVPDVVSLLEQINTPPGTWYAAIDLANDFFPIPVHKAHQKQFAFRWQGRQYTFTVLPQGRWEINMTKIQGPSTSVKFLGVQWCGACQDIPSKVKDKLLHLVPPTTKK/EAQCLSGFRREHIPHL\PIYRVSRKAANFEWSPEQEKALQQVQAAVQAAWPLGPYDPADPMVLEVSVADRDADWSCWQASI/GHKVGHAQQHSIIKWKWYIRDWARADPEGTTKGQGQRRWWQLAERQDSRDREAAIGERQETAVGKTARDGEAVCD
3629	33997	A	3669	349	718	AGPEGTTTAECP/I/CQQQRPILSLRYGTISWG/DQSATWWQVDYIRTLLSWKWQSASAKTTIHGLTKCLIHHDIPHSIASD*GTCFMAKEVWQWYCFSHSQDSRVQESRGGIGSCTTHHHPCSFPN
3630	33998	A	3670	667	960	
3631	33999	A	3671	1	1371	
3632	34000	A	3672	1	942	MVGKAKWKPLELPLPRKIVNQKQHHIPEGIAEIAATIKDLKDAGVVIPTTSPFNSPIWPVQKTDGSWRMTVDYCKLNQVVTPIAAAVPDVVSFLEEINTSLGTWYAAIDLANAFFSIPVHKVHQKPFAFSWQG/QQYTFTVLPQDYINSLAL*HNLIWRDLDYF\LLLQDITLVHYIDDIMLIGSNDHKVGGAQQHSIIKWKLYIHDQAQTGPEGTTTSVIAQWAHEQSGPGSRDGGYAWAQQHGLPLTKADLATTTAECPVCQQQRPTLSPRYGTIPSLPLTKALTLQLKKCSSGPMLMEFTGLAMFPIILKQLD

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3633	34001	A	3673	1	1270	MGDPSRRRTCRAMQAKYPLVFKGCGVCWGSLDPRCRVASQVWPIPKRLSRGWPFHNAVGRQVSDWKSGQDFADFGTTHQTGFSPAGANQRGPLAATLSGPGGEGQSAVARLTGEKKNHPGAQYANRLSPRVGRFINAAGTTGFPTGKRAVSATQLMILCLLPGYLCNGKRKLSAIQGLLDNGSELSLFPENPKRHCGLPVKVGAYGGQKTDRSWRKTVDYCKLNQVVAPIVAAVPDV/VVSLLEQINTSPGTWYAAIDLTNAFFSIPVHKAHQKQFAFSWQGQQYTFTVLPQGRWEINMTKIQGPSTSVKFLGVQWCGACQDIPSKVKDKLLHLVPPTTKKEAQHLTGLFGFRRKYIPYLGVLLCPIYQVTRKAASFQWRPEQEKALQQVQAAMQAALPLGPYDPAGPMVLEIAVADTEAVWGH
3634	34002	A	3674	1	1978	LTIYAVNLSLILPQGDLWPFTRVTVH*GKGNDQTFQELLDTGSELTLIPGYPKRHCCPPVKVRVYGGQVINGVLAQV*LTVGPVGPRTHPVVISPVPECII\ILSSWQNPHIGFLTGRARAIMVGKAKWKPLELTLPRKIVNKKQYHILGGTVEISATIKDLKDTEAVTPTTSPFNSPIWPVQKTDGSWRMTVDYCKLNQVVTPIAAAVPDVVSLLEQINTSPGTWFEWSPK\KALQQVQAAVQAALPFGPYDPADPMVLEVSVADRDAIWSLWNAAIGESQRRPLGFWSKALLSSADNYSPFERQLLASYWALVETERLTVGHQVTLRPELPIMNWVLSDPSSHKVSGAQQRSIIKLKWYIHDWVRAGPEGTSKLHEEVAQMPMVSTPATLPSLSQPALMASGGVPYYQLTEEEKTRAWFTDGSARYAGTTQKWTAAALQPFSRTPLKDSCEGKSPHHPVIAQWAHEQSGHGGRDGGYLWAQQHGFPLTKADLAMATAECPICQQQRPTLSPRYGTIPQGDQPATWWQVDYMGPLPSWKGQRFVLTGIDTYCGYGSAYSARNASAKTTIHGLTECLFHCLGIPHSIASDRGTHFMDKEAPSASVLGLALALLAPQLADSLLEDPVIVKGTDEAEYFQSVREEPDSGVKRKKMLKSGKNY

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3635	34003	A	3675	1	746	MGKIVQPEKAVSAKAGVCLKGCDCSEYKVQCEWQDTSPKYLGIVLSFGEEPVTHLRWDLHAWSYALSKVISTICRRGKFSEFKAHTAPVRSVDFSADGQFLATASEDKSIKVWSMYRQRFLYSLYRHTHWVRCA\KFSPDGRLIVSCSEDKTIKIWDTTNKQCVNNFSDSVGFANFVDL*PPSGTMP*PSAGS\DQTVKVWDVRVNKLPTALPRMVYYGAKCHLWGCWSFTENSELSFQLFCTSIPIWF
3636	34004	A	3676	5	812	AAGSAGLPATPQPRARRVGRRRLGPGARGAGGAGGAAGCRALRATARAAGSQPGPHSPGRTARSARK*RLRRPESNKVRVCGPHSPAPRTPPSSPGIQHAGKPRARRPLPPPGAGVGLGIVPGLGLGRAGADVAGRVGPGAGVPGCCREGARRPGSGRRAAPVLSPLC\PGLQTARAAAGPAPGA/GWP*VRRLEPAEALPSGMFMMRKSCSVALTSSLSSSPSSSSSSSSSSSPSLTRPDVSPRVTAATGDMYRGSFSGLTKALRTWPR
3637	34005	B	3677	1	1071	
3638	34006	A	3678	1	169	
3639	34007	A	3679	2	189	
3640	34008	A	3680	3	352	SKHNLKLTATSQPHRPMQLKPACVPPVLSSPHMWGRSDTSEGPAH*PPA\AWRVCVVLGL*ASPPAKLQAQHQAGSTRPVDRQAPSVLTAPPLVWPPFPQGICSKWGAQHGKRGQGH
3641	34009	A	3681	8585	9026	ERYKFFSAASPNILILLTFFKIVVRPLITKENLYLEILIRHSLLCSVLTLVCVFCCPVFIGSCSSKRLTTAWTHSTGLCAAMSSPRPGGGGGKGGPAPWAGKRAGSGG*GEGRGKERVCGVQAPSVPTGVGMGGQRRAGVGGPRAAP
3642	34010	A	3682	2	484	
3643	34011	A	3683	1499	1793	IHSIESSPIPHWIGGLRLMLCIVTRLNFEICLVKHFIKQCKVVEHTQQYEWHRVLHLKKK*QALNLKKNLQT\GDKKL*VSSLVHGETNSCRSKALAL
3644	34012	C	3684	1	1044	

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3645	34013	A	3685	8504	8970	ERYKFFSAASPNILILLTFFKIVVRPLITKENLYLEILIRHSLLCSVLTLVCVFCCPVFIGSCSSKRLTTAWTHSTGLCAAMSSPRPGGGGGKGGPAPWAGKRAGSGG*GEGRGKERVCGVQAPSVPTGVGMGGQRRAGGGEGKGALARRLGGG
3646	34014	B	3686	1	2178	
3647	34015	A	3687	1	2424	MLTVIHSEMQAAKVSDGNEELIGKWNLLGIERPWGPRRDWSGLHGPGPGTPTARPRPLRDSSQNTWRLQLKPRLKGGPGAQNARMNEAWQPLPRFQRIYEKTWVPWQKHDAGAEPSQRTSTRAVPRGSMELEPPHRAPRAVRRVPQFSRFQNGRSTSILHPVPGKAAGTQLKPVRADLVAALYKATGAELPKALGAHPLHQCPLDVTDELLEKIASRSQNIIEINISDCRSMSDNGVCVLAFKCPGLLRYTAYRCKQLSDTSIIAVASHCPLLQKVHVGNQDKLTDEGLKQDNQPQCIEGNFESRMHAQGRTLVQERPKKTVNFITVCLLGPVQAGSKGQGRVVNGKVLTSTANLRRISVDGKSEKSVKDAEKAFDKIQQPFMLKILNELGIDGMYLKIVRAIYDKPIANIILNEQKLPWVVDGTGRCGAGGSVTGEARAMQ\GPQWGKGRLRHGGLQVPIPALQGGS*GPARN*AQQLLAQRIKYL*IQLTRDVKDLFKEN*KPLLKEIKENTKKWKNIPCLWI*RINIVKIAIL/PKVIYRFSAITIKLPLTFFTKLEKKTTLNFIWNQKRACIAKTILGKKNKDGGIMLPDFKQYYKPTVTKRAWYWYQNRYIDQWNRTETSEITPHIYNHLIFDKPDKSKQWGKDSLLNKWCWENWPAIYRKLRLDPFLTPYTKINSRWIKDLNVRCTTVKI

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3648	34016	A	3688	453	1508	KAPQAPNINSYCLQVEECCQKG ISVDLSTGMTSTGVVP/HYNEQ VAGEKEEETNSVATLSYSSVDE TQVRSLYVSCKSSGKFISSVHSR ESQHSRSQRVTVLQTNPNPVFE SPNLAAVEICRDASRETYLVPSS CKSICKNYNDLQIAGGQVMAIN SVTTDFPSESSFEYGPLLKSSEIP LPMEDSISTQPSDFPQKPIQRYS SYWRITSIKEKSSLQMQNPISNA VLNEYLEQKVVELYKQYIMDT VFHDSSPTQILASELIMTSVDQI SLQVSREKNLETSKARDIVFSRL LQLMSTEITEISTPSLHISQYSNV NP*RGCFHYCLAFT*T*SNTLSI YSENVQEGLVKGN
3649	34017	C	3689	57	230	
3650	34018	A	3690	2	123	WWKV*KKYSGFKVFL*HQH** PRRPLQSLFS*MPWKRIAK
3651	34019	A	3691	94	360	LMSLLTSPHQPPPPPPASASPSA VPNGPQSPKQQKEPLSHRFNEF MTSKPKI\HCFRSLKRGVSSAPE SCLSGVLWLHVWFCITNFVCE
3652	34020	A	3692	1	2037	
3653	34021	A	3693	2	1079	NLSKKYQPKKNSKEEEEYKYTS CKAFISNLNEMNDYAGQHEVIS ENMASQIIVDLARYVQELKQER KSENDHRVSGASRRAPLPGPFR RLRPFTPDVGGEEAAANQAE\Q *YPSLKWNSKGKTNGTRNGTK CGKEHSPTLHQSRQGTVIQSAN RPSVA*SYRAPLHPSPH*KLAP* VPAFSSSRVFPMLSSFSL/YISTD DQEGLYSLYFHKCLGKELPSDK FTFSLDDSQLVIEAYKSGFEPPG DIEFEDYTQPMKRTVSDNSLSN SRGEGKPDLKFGGKSKGKLWP FIKKNKSPKQQKEPLSHRFNEF MTSKPKIHCFRSLKRGIQPPDG NEKQDDTMASSFTFSLSLDYEM PVIEKAE
3654	34022	A	3694	1	215	MAQDYGAMGDLVLLGLGLGL ALAVIVLAVVLSRHQAP/C*PPA FAHAAVAAHSKVFSNIVRERV KTQEAERA
3655	34023	A	3695	1	208	MAQDYGAMGDLVLLGLGLGA\ ALAVIVLAVGLSRHQAP/C*PPA FAHAAVAADSKVCSDIGQRTC RDATPT

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3656	34024	A	3696	1	164	MRYRYIPVRMAEVRT/SDETKCW*ECGATGTFIHCWLANIQQHTLSRLFTCLCSC
3657	34025	A	3697	146	659	LAGPRCTTSLTPSEGG/LPPPDSLGYTVHPPDSQGHTGPLPAREGTGSHRFGVE/VRQRRWERGEAPLLQLSPPAGRPPRRPHPCRPQHLPSAAISEAATARGPRNRSQAAAAAADPDNLRVARG/PRSTRSSAVDAGPPP\SASPGFP*SSSQQRPSPEKTGSEVYSAYIPANC
3658	34026	A	3698	32	376	
3659	34027	A	3699	1	2148	MALSPWTPGLGAGEKLVQAAAVSTGPSLELCTLPSTLGSSVAVEALEQLFVVECVRDARRLNLFEINTIKMRITRTENEIELLKKKITDLTKYNEALGEKQEELARKHARFVLSLNQTMEKKATITVYINETYTKINLKREDIALQKKCIQEAEELMEKERAEYLIRKQELTAQINEFENTREVKRMETYQKK/QRIG*ITN*NVKNKRNSY\FSAAVLSDHNLEIARLHESIRYWEQEVSELKKDLAILEAKLCFFTDNKEKLDDISNDEKNEFLNKIKQLVETLHAARMEYKDLREKMKTLARQYKIVLSEEEKAFLQKQKIHDENQKQLTFISQKEYFLSQKRVDIKNMEEGLITLQELQQVILSFMSSVYSKPNLSHSRGLTCCSFPLYLQMMTPFPCVITQWKMACLRKKHARWTAKIKAEIQAITEKIQNAEVRRIELLNETSFRQQEISGFVAQIEKLTTELKEEEKAFVNKEKMLMKELSKYEEIFVKETQINKEKEEELVEYLPQLQVAEQEYKEKRRKLEELSNIITEIIWGFLFEQEDVKQELQQLRDQESKKNKDHFETLKNLENGFYINDQKADLLLLENKKLKEYILYLKNNIEKYREGQEALMHTSSDLSRQLIAQEGLLQVEEQGIQWWIRQSPKASQVGKPTVQPSVCGQRPKSPCQTTGVNPRVQKLKNLESNVRGQEASSTGERGIL

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
3660	34028	A	3700	1	2658	MQAPYRCQRTGWLQQKRLKAGLWGLESSSWSLGPLGQAAQQELTSAPGQFRLPPPPQAPERPTAGGSASLGPPLP/PGKLSEVPEPSRPGRPRRPPSTWAPPGGP/GASALPVVPG/HRGARTRGASTRGAS/EAGPHLPIPVTSNAPGHAGGW\GAPSHQNHASPCTGRGPQPAGELRQA/GEQFPNSWGRRGSCRTCSVVLGHTEPRPEPAHVLVR\GNPGSPVGAAWGNEA/GHPRAPGAQRGG*RSPGLRE
3661	34029	A	3701	31	556	
3662	34030	A	3702	3	1394	RKKELQHKIDEMEEKEQELQAKIEALQADNDFTNERLTALQENQTRAKESDFSDTLSPSKEKSSDDTTDAQMDEQDLNEPLAKVSLLKDDLQGAQSEIEAKQEIQHLRKELIEAQELARTSKQKCFELQALLEEERKAYRNQVEESTKQIQVLQA\QWQRFHIDTENLREQKD\NEIASARDELHSARDEMWLVHQAAAKVASERDTDIASLQEELKKVRAELERWRKAASEYEKEVTSLQNSFQLRCQQCEDQQREEASRLQGELEKLRKEWNALETECHSLKRENVLLSSELQRQEKELHNSQKQSLELTSDLSILQMSRKELENQVGSLKEQHLRDSADLKTLLSKAENQAKDVQKEYEKTQTVLSELKLKFEMTEQEKQSITDELKQCKNNLKLLREKGNNPSILQPVPARIHRPIPGFPDMVIRSIVERKKPWPWMPMLAALVQVTAIVLYVPGLARASP

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3663	34031	A	3703	1	1133	LEEKEQELQAKIEALQADNDFTNERLTALQEHLLSKSGGDCTFIHQFIECQKKLIVEGHLTKAVEETKLSKENQTRAKESDFS\DAVSPGKD*GSDDSTDAQMDEHDLNEPLVKVSLLKALLEDYRGGYRNQVEESTKHIQVLQAQLHRLHIDTENLREEKDSEITSTRDELLNARDEILALHQAAAKVASERDTDIASLQEELKKVRAELERWRKAASEYEKEITSLQNSFQLRCQQCEDQQREEATRLQGDHTDEAADLPLSRHSVSDPGVSCTQEEIQEARGLTLLCFSKIKCSQKQSLELTSDLSILQMSRKELENQVGSLKEQHLRDSADLKTLLSKAENQAKDVQKEVKRKDIMSPIMVGLKAKS
3664	34032	A	3704	1	540	
3665	34033	A	3705	1	280	
3666	34034	A	3706	2	416	
3667	34035	A	3707	309	908	LPSRGAGLGTCRPPCLSLPLLPWAPVLPEPPRRVPPPAPRRPVGSTTQGLRSASTRR/VDWQAAPPAALVWDPLGEASWAP/GVWCAAIDLANAFFSIPVHKACQKQFAFSGQGQQYTFTVIPQRYISFPALCHNLI/RRDIDCFSLLVVHFAWKEKWSDVRLGTDSWAAASGLAGWSGTWKKHDWKTSPLVIHEQKFCFLFP
3668	34036	A	3708	1	2973	
3669	34037	B	3709	1	1053	
3670	34038	A	3710	1	1178	
3671	34039	A	3711	3	247	DCLRVLWCPPV*F/QRSPSLQQPL/RPGFEPLVGRHLMRPARSWRPQPSSASAGLPSSPFRDGCHRFRASWALGGRAAEGEVAI

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3672	34040	A	3712	137	2176	LKNPPQTHPRRGHLLLISVWGHILRACGAWQEAKPKAKWPQIPEEKEEGQAPRACTLPGCWRLLRRGQEEKEENWVPPACTLSGCWRLEAVRQQQREGDGDFGAASCSDLAFRCASSQNPRSLEPVASSPERRRRQPSRAPLGWALKEPGSERSPPLLSCVEALQPPFLLGLGSGAFCLTRGEKGSPDQDPFCLHSPWMLEAGGSDAATARGDFGAASYSDLAFRCASSQSPRSPEPVASISERRRRQPSRGFQILRSSGAFLLDREHVCLASSASTTGLGSPRPSWSHQVASNKGLKPGLRGCWSDGERGTTLEDTRVLLSNPLLLRKGGRKVSTSRLMQLCSVVEKYCPWFLDQGTMNIEIWEKVARALKKAYRDGAEDIPINIWSVWALVHPTLEPFHTDHDEEESEEEGEYNEVTKEVTEQFCLPAKAAKEGGNPSLTSPQQLTTETEAEIQLIEKQVHKAQINRIDPEKTLDLLIFPTQHSPTGGVVQEQDLVEWLFLPHSNSWTLTPYLDQIATLIGNGRTQIVKLHGYDPGKIIVPLTKAQIQQAFINTLNWQTHLADFMGVLHNHFPKTKLFQFLKLTNWILPRITKFKPIECSENVFTGRSSNGKASYSRSKNKVFQTSYTSAQKAELVAVIEVLTAFEMPVNVISDSAYMAHSTQLIE/TAQL*FHTD
3673	34041	C	3713	1	784	
3674	34042	A	3714	87	447	AVQRRSGVGPACLSCGSANPGPPPGTSPGAGAAPGGGRWARAKSGPESPPGT/GPPQPA*APQ/AAGPKTRAGVSFLSPPLASSPGHANFGPDSFLGDGVMRQA*RSENKQDPA\GTPGTWVR

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3675	34043	A	3715	3	1435	RGPSGPRTVSPSPAGASSVGGPPVQAWPCSLCVGSLEPRGSIGGPPKGLQLWGPRASWFLGDYACPLLASAPVLAACKTLCQTPAVPASL\G*RPLVAVKTHVAAQPFLRIKHLAAVLADKSAPGLRPVCGTA/GFAGYLCLPHSLPSPDG\EPVDVSTLDSAEYCQLGLGGICRGPGR*EGGHGY/RGSEKPHSTYPSSPSLSG/EPENRG/DPGVAQEP*PPPREQAGPFSPFVILEAAPFSAGACFPGSEAPGGSSPPN\GSAVGLWRGRCPPGPRSL*RIAAAWPEKRCLDSWKG/RRDGAARGVGTAATFSPPFASRLVLPGEASLGTPGVVFLLRAGEPSASGFPGPAWRESTAGASGGGCCGHGPCSGLRAAGLPSGAGSW/RGDCCHLGMGEDPLG/PW*SSGTPASARGSQEVPAT*GRAGGRAARHPQGARLPSGPPG/EPGSPGFWHRKESQSTLTFLGAQGSSSPLADLGSLGASAG
3676	34044	A	3716	1	756	MNDAGNHHSHQTNTRTGNQTPHALIHKRKLINENTWTQEGEHHTLEPFGGTTDRIVSPSHTRSPDMAIANFQSSGCSVVPDTIPRPQYQCRSRHSVLLTSNLTVPMQSCVKPPYMLLVGNIKIWMNNQTVRCINCHVYTCITSHFDSRKSVMLVLAREGIWILVTLPRPWESSLSIRLINEVLQRILKRSKRFVFTLIAVIMGLITVTALATTAGMALHQSVQTAHFANDWQANSNQMWNSQQGIDQ*EHMDTGRGTSHTGAFWWNNRQNSFPFPYSQSRHGNSQFPKFWVFCCPRYHPSPSV\QCRSRHSVLLTSNLTVPMQSCVKPPYMLLVGNIKIWMNNQTVRCINCHVYTCITSHFDSRKSVMLVLAREGIWILVTLPRPWESSLSIRLINEVLQRILKRSKRFVFTLIAVIMGLITVTALATTAGMALHQSVQTAHFANDWQANSNQMWNSQQGIDQILAAI
3677	34045	A	3717	3	131	

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3678	34046	A	3718	2	424	CGRKSRGTALPTGSSPQSGPAAPGHSAASALHPTP/SPPPHPL\PPAATGDIDGNRYPATPMTKYPSASARRPVHRPTCSGGGSHTNHAESLPPLTPLEEADTHPPGGSQ*TRPPHCIRTGSCLPPPREAPYTRRERRRHPP
3679	34047	A	3719	1	418	
3680	34048	B	3720	361	1371	
3681	34049	A	3721	1	469	PGTCRGSTGQP*EACWRSP*SVRNTRCPVREEPASPGWSSCLTSPSARGWWACS*RLPSSSCPGSTAGSSSGTLCREAAPCHR*AACSDGKPPGMPRSTRRLGPSGARSGSARRCPCGDGPESLRGHAPARAATQAPDPSTQSSASSATPRAPPLL
3682	34050	A	3722	117	871	GPQSSAGNAGPQRRRTTLGVPRTWHPGPAA*AGNSCHISFYSSRFQPFLGVTSVLRGSSVSVSGIPDHLGQPRSSQEPSRPENAAAQM*TGCPGYAGCTVA*MKGRAELQGLRTIAAQPGQWLTLLPRCPSTRRLGPSGARSGSARRCPCGDGPESLRGHAPARAATQAPDPSTQSSASSATPRAPPLLGLCGGGC*GDRRSQQGTE*A/VAVPGMLGGPSPFSQPEHPSAFAQPSSCLPLGLDFKLLIPSQ
3683	34051	A	3723	110	1017	EAANEPKHLHQLRHAGLGQHRQAPRPQGRPFARPHQGQDQTDRLHHLQGGGRHGARGHLHQAGAGQSAPAPKGAHVQGPCGCHESTGPVEH*SHGERPKHRCPRPAL*EHGHENPHK*SSPHDQR*QTADPEGDN*SQCCPTAN*IPLRKLWLRG*DLCGRSHGQQ*PHQGW/HLDAQLLTPASSSTLCPTPLQQPLHQLRHAALAQHRQSPPAART\PLARPHQGQDQPDRLHHLRGGGRHGARGHLHQAGAGESAPAPKGAHVQLVSKQLGGVAAEAHVDSSGLWVSPGPRHN*YKSKSSRL

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3684	34052	A	3724	3	1092	LVEPGRLLEAQGFDKNKR*RRRGRVCGRGGEAPAPGQGQGQPD*NKGKEEV*NSSE\EESSEVSLPKTSREQEIPSLACEFKGDHLKVVTDSQLQDDASGQNESEMFDVPLTSLTISNEESLTCNTEPPKEGGEARPCVGDSASTPKVHPGDNVGTKVETPKNFTEVEENMSVQGGLSESAPQSNFSYTQPAMENIQVRETQNSKEDKQGLVCSSEVPQNVGLQSSCPAKHGFQTPRVKKLYPQLPAEIAGEAPALVAVKPLLRSERLYPELPSQLELVPFTKEQLKILEPGSWLENVESYLEEFDSMAHQDRHEFYELLLNYSRCRKQLLLAEAELLTLTSDCQNAKSRLWQFKEEQMSVQVF
3685	34053	A	3725	182	771	QTALSCARHGRSAAFVWRPNRAPVWRSGFRGVAAGSALVHSTALPSRRQPPERRSEHDCLRCRALCGTKPQGLSY/TGP/WGLGKVPEAAAALDLGVH*PLFHLPLLDSESRKPGRGLAAPPPMPARWGLSCLEQVGHTRKEGGGQGCRPWPPCWSPVSGTRGGPITTRLRRGSAALHVRASYCLMENPPEPPSIV
3686	34054	C	3726	769	981	
3687	34055	C	3727	70	197	
3688	34056	A	3728	1	158	LGSVSSFASCTLGAPGYSPTAPVAL*SVGPWGRIVKVPGHPGSWEMHFIISM
3689	34057	A	3729	229	496	VTGLQNLVLSIVTESGKTHLLSFSSHGLEEIISQLPGCSGTLTVRPQGPT/GSQGNRGCDRVAQGSQGAGGERGDRSQAPVPAPARDS
3690	34058	A	3730	167	769	FLTRETGDPTGRSSSHGKHPVAVFP**PTRPP*TIWEITHGCGRRAGRCPGTGPDGP\SGRGGPRCWPSGHLAATGGLGPSCGRLGANRGEAGPAGFTVCSPLSGWRTPYTHHFPASRMSWHLDYASPRTYRSQGNRGCERVAQGSQGAGGERGAGSQVPVPAPARNKDPAKRQKPRPPLLSSPTARLIGLFPRADSCRSC
3691	34059	A	3731	234	543	ALDQVASLPIMVPASKQNTATSCCRLGYNSFDLGPAAATIFFPSPAMVISQLPGCPGTLTMRPQGPT/GSQGNSGCERVAQGSQGAGDESGDGSQVPVPAPARD

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3692	34060	A	3732	1	3695	MGKRSFERVLVDKCDSGRSCLRKQHENECAFIQILDTQSLMIPGQRGSFRLADSQHTDRVLCTLMAEKWDRKALSYTRNSFRAQIRLRKTRFQGKGCMICKKSRVLPYQAAYVSQHGSACQPSSHLPSVGSLSSTGDDEEEEEIVHMGNAIMSFYSALIDLLGRCAPEMHLIQTGKGEAIRIRSILRSLVPTEDLVGIISIPLKLPSLNKDGSVSEPDMAANFCPDHKAPMVLFLDRVYGIKDQTFLLHLLEVGF
3693	34061	A	3733	1	2523	MKQFLLYLDESNALGKKFIIQDIDDTHVFVIAELVNVLQERCHTRLGYTEFLVAWRVTFGLCVEAVTLHLKYQILIRGLLEMMSFSDADILKQLPVTVPGLFPASLSPSSLLGNSPPSWLRHNSESKVSAVSSPSATKTLSTGIGKLDPGHKEMAEESELLKNKMQAPPLSRCPESQKCQHQLRLHHWKPSVRHQVKRRSPAVLRSAMPPADCPAVLEATTATHPEKGTALSKHLPSSDSMSLKVDVEALENSPGATYIWKGGKVTRDSQPKEQGKGDLKKKKKGKLPKNYDPKLTPDPERWLPMQECSFYQGRKKGKKKDQMGKGTQGATAGASSELDARKTVSSPPTSPRPGSAATLSASTSNIIPPRHQRPAGAPATKKKQQQKKKKGGKGFPVLREITVVKVDTLVVFQILEERLSVFHIQYDTSYPFSTVDIEDHECAVWLLLRKSKSDDKTTRLEAVREMSETHHWHDAEKAFDKIQQPFMLKTLNKFGVDGTYLKIIRAIYDKPTANIILNGQKLEAFPLKTGTRQGCPLSPLLFNTVLEVLARAIRQEKEIKGIQLGKEEVKLSLFAGDIIVYIENSIVSAPKLLKLISNFSKVSEYKINVQKSQAFLYTNNRHTESQIMSKLPFTIATKRIKYLGIQLTRDVKDLFKENYKPLLNEIKEDTNEWKNIPCSWVGRINIMKMAILPKVIYRFNAISIKL

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3694	34062	A	3734	1	6208	MILDQAFKYITELKRQNDELLLNGGNNEQAEEIKKLRKQLEEIQKENGRYIELLKANDICLYDDPTIHWKGNLKNSKVSVVIPSDQVQKKIIVYSNGNQPGGNSQGTAVQGITFNVSHNLQKQTANVVPVQRTCNLVTPVSISGVYPSENKPWHQTTVPALATNQPVPLCLPAAISAQSILELPTSESESNVLGATSGSLIAVSIESEPHQHHSLHTCLNDQNSSENKNGQENPKVLKKMTPCVTNIPHSSSATA
3695	34063	A	3735	164	415	EYWGWLLRRINIILTGNCLRG/WPSLLPQAEESLSPQTKVERLKAAWIEEGILPLLGMRKLFLLARKVHQSLQAQCPQLHQGPPT
3696	34064	A	3736	1	886	MLDLPWFNVEEGIQRLREIGMLEWLSHFRPTRLSREDPEDIPFTNTLPNKFVRGVPASLKSSFIGLLCMPDLTKTVGSWRMTVDYHKLNQTVTPIAAAVPDVVSLLEQINTSPGTWYAAIDLANAIFSIPVHKVKDKLLHLAPPTTKKEAQCLVGLFGFWRQHFLHLGVSLWVIYRVTLKAASFEWGS\EQEKALQQAG\QAAVQAALPLGP/HKDPADPMVLEVSVADRDAVWSLWQAPIGESQQRPLGFWSKALPSYADNYSPFERQFLAYYWALVETERLTMG/HQVTT*PELRIM
3697	34065	A	3737	1	1815	
3698	34066	A	3738	1	988	MPAEFFQRCSVIMVQLPWKEAHVERPHGERDYTPDLQPDMWEKFPGLRRALRPVVKTLLVQLEYRQAEKCEKRDWPSLPDYIFLLCWMLPALEYRTPSSSVLELRLALRAPQPADSLLWDLVIVPITSLKSWQTPRGEVEGVTHEEICASLKSLAVALLSMSDLTVGTPVTQPQTLNTMGIIGSRGGRGQVAALNRQRQVPELIIGIDILSSWQNPHIGSLNGRGYINSLALCHNLIRRDLDRFLLPQDITLVHYIDHIMRLDSVKDKWLHLAPPTTKKEAQCLVGL/FGFWRQHISHLETAL/RPVTGLWWKLNI*LWAIKSPCNLNCLS
3699	34067	A	3739	26	318	RTAWMQYSPLHSAYGRVPTVTSSH*LLPLRSHPRDSRPAPCP/RAGPARNRQSSA/SRNRSPRRRNPEASRGRPPGRGVASPAPSPPTPRETRTAATRRP

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3700	34068	A	3740	425	588	IWSVPFAPWRRRGHAGSRCSRRSRSR/TPRRNELSTAALGAARGHARIWREAGNWP
3701	34069	B	3741	465	1623	
3702	34070	A	3742	667	960	
3703	34071	A	3743	1	2021	MTVLTQTSSQHSTGCHAKPAITTPWLLAVFFQGPGVLQSVGGKASQADIILGLSPVSAIFQLYDVSFPPGKQGRPGLGSAGRIEVARDCGMLWKQRGYLISSSQPIKNGQQVSDLFEAIPEPKSLAIIKISGYSTLETPESKHNHFTNTLAAIDLVNAFFSIAVHKV\HQKQFAFIWQGQQYTFTVLAQGYINS/PPALCHNLTQRDLDCFWLLQDNTLVHYIDDIMLIRSSEQEAANTLDLLVRHFCATGWEINPTKTQGPSTSVKFLGFQWCGACQDIPSKVKDKLLHLAPLASKKETQRLVGLFEFWRQHSPHLRMLLQLIYQVTRKAARFEWACTDGLMRSPYDQLTKEEKTRARFTDGSTQCEGTTQKWIAAALQPLSRTCLKDSVHQRVSSAEEDFNNQVDRMSRSVDIIHPLSPATPVITQWVHEQSGHGGRDRGHAWAQQHGLPLTKADLAMFTAECPIFQQQRPTPSPQYGTIPQGDQPATWWQVDYIGPLPSWKRQRFVITGIDTYSRYRFAYPSFNASAKSTIHGLMECLIHSHGIPHSIAFNQGTHFMAKEVWQWSHAYGIHWSYHVPHYPEAAGLIELWNGFLKSQLQYQLSDNTLQGWGKVLQKVVYALNQCSIYGTVSPIARIHGSRNQGVEVEVALLTVTPNDPL/GKY*LPVPVTLHSDR

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3704	34072	A	3744	3	1197	TLGPGTGPRAGTGSSSSPSSSPG TGSVPGAGPGANSVVHPGADS GVRAGAALAPGLC*VKLLGQM SPPGGALGPHNARQSAVAGGF GRARRPGRHE*LQGTWWSGPG QPLGAALQTATGPVVMNQFLR *TWHHEGHSRAPCPRFWGWF* TYSGEKPLPAAVQPSSSSVF*SL QQRCPFFLGVPCQACSSACPLL F*GL*W*PGVHEDQ*ASPAGSA LTWP*LHHDPPPSSGA*SDATG PG\GPGSALAGFQQLGSGGQVL QQGQLGSQTCRGGSPRGRRHC* ASSWG*G*AGRLLPWA**PPAR SAGSPHRLRGLS*ARPCGCAPR CRAAGGAGP*SSAPRT\GDGDV GQLGERE*EAHPARVGQWGW GSRCPQGQGVAFSGSESYMDW SSRNRRFRNT
3705	34073	A	3745	1	98	
3706	34074	C	3746	439	1053	
3707	34075	A	3747	48	751	EGDLVFPLGRGMLRLVSFSKMF KLLKRTMDYGSGSPSVSGHIPL PQACGPPQLVCSRRVRGQRPRP HSVPGSRAAPGLSGDTGRFLSG FGKFCFGSRKGALLTKGFSVSS GWPAAKFPPAQRVQTIVRSR\P RRPGKRVL*GEK/GEWAASLPT PLPLAGPSLPSVPGPVPVAPQTV RAVSPVTPQGPSSPPFLREHSTQ PRPGCREIYQHPRMGTGRMRTP WPWRLSARPAAAAA

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3708	34076	A	3748	1279	2791	QAAGGAAGAERDEGAGVA/GAHGPSRSTARRGGRGAGPRPPPPPRSLGTGSAGRGAAEGTGRARRPAGAAAGRALRAGRAGRLGACGGVAAVGARGLRAAAAGARRRGAPATGAPPP/PSAAASPTAP\PGPRHPGRVSGAAARAPPGTAPRIGERRPGGGAPATEPPDSRTPAAARASSA/PGAVSGPAAAPGPPGRRENAEGR*PQDAG*RGLWEGALPVPGSSPQTSSSSTGRTSGGSRAPSHMVPGTGSPPG\RGGEAGAR*AAAPAGVKPSSLWKK*LALFRPCFQEPTPG/SVGCRGPLECFTHSSPVGV/NGHRHCDNCCR/PLKPPSPKAAWAVPRAAVPEAHA*K*RAEDQRGLRVLGPNVTLSNPPTRGFR*LGTGVPGFQDPCVDS/GL*VEEGLCPEASRGNGERNKGTWGIPPQPPLRPSSRWLQE*PTPLPGSP*DATSPPAGGGRHRSRLPKPALVGNAGTSSLPAPEPCFPHLYFTTFLLSLDSSLKFRDLAGILIPE
3709	34077	B	3749	71	285	
3710	34078	A	3750	417	1208	GPQRVPTLWWEDAEARSQRDGVGGRAEAPGARIPRDLGAAGGLRGHPRLVRGHCRRRLRCSMARTLVLRVTPVPGGAPLALRQPPVPGGSRQEWPAFSRVGTGLPLTPTAGPSRARGARRPCPPALPGHCLLDRTYTGLQTLGAETLLAVVNSAAMNVGVQVVDVELHRHSLGEDCIYPQSSESDISDAPPSLPLTIPAPVKASSPIKQSHEPVPDTSVEKGS\PGSCPFHL*GPLSHLGSSPGFLLWRPPGLLSSVALVASC

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3711	34079	A	3751	10	932	LQLCSMWLLRSWVQAEGAVSI SDSPFSLHQCWAVLHKAWCVF LQLPGGFTFTLNPLSDNLLGKR VDSAPSWGPLGSAFRGVHMPC VGAAWEGKGPNLLRPSGKLGP SGSRPTPIGQQQLPEVPRAKGPL GPAAVICQ/HMPAPSTGGKRGS FSGRYLSASLELGGLPMAPTGP SALSAPPSVSRGAR*STREKPGV YASAT*AAEIREGQALGG\PRPS RNG/SGGPLGPDFGPNGPKLRRS KAGCPWWHLSSVDAGE*LWK QHSTAVFSMPGTQPPWRGLITM PISPRGTEPTAHPGPRSPGLAYS LTA
3712	34080	A	3752	3	650	GTVLDDPHLTGYCWHPPCPPNS VCNGSLSPVLREEAESSEAPVQ SPQRSWTPSAKSPPLPASPPCSQ LKAGGDQEGLQRGALPVGMD RGGPGGCGGHCQCSRPRILSPV VPVPQVCPSSEAPGPPRQVPHTP RPQEPSRTRGRLEA\SAPSWQ*P APPAGSLPAWP/PG/RPAPTGSR AR*AGLEASETTWSTNGPTTVH P*TL*AGSLGAPQTSAAASEHSP CPNLPLPL*KPWCATNLSCRI
3713	34081	B	3753	1	1812	
3714	34082	A	3754	1	209	MAQDYGAMGDLVLLGLGLGL ALAVIVLAVVLSRHQAP/C*PPA FAHAAVAADSKVCSDIGQRTC RDATPT
3715	34083	A	3755	2	462	PPLPGCLGDTGAPWPGPGCTGP PPRTRSPPRLPG*APASRLQNPH PRGRPWPAGHSRCH*SQPWLA GPTGS*HLPDASGFCPGALTGS CLPSLGGAGGGW\QSAPPDVGS KWNTPRRSGAPAPPGGRLLPGP ACRAPPRSDLPLS*AGRVGRPG
3716	34084	A	3756	129	616	NRIFLNCNMVHKCKCKTPMVV AGASLVETGQDESIKDE*LNGIP GPVATPSRLPPQRTWN\PGPHP MP*RRPQSLPQPSQAPPGPFLS* GSEGEGTQPKP/P/GLPGLGPPR QPGRCGFAVD/PPRCGVSPGPG VPGPAGPAAGAAPG*PKLRQRP GPSIGDCGDAP
3717	34085	A	3757	59	292	YCNVSFGPILSARKPASPRSS*T SATWLQNHPLMYLTPGTGTLW RFLTTRENVPYGPVP*WNRTIC GVANWPYWPSV

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
3718	34086	A	3758	177	448	GTGGWVAMLQQYFA/TAWIPHNDGTNNFYTANLANGIAAIGYKSQPALWVTGGLLVIIITFIVRGIVYPLTKSQY\TSM\AKMLVL*PGAEGL
3719	34087	A	3759	1097	1206	
3720	34088	A	3760	2	505	QGSRAKLSTPLGLSCTRSTAGPSRFARCSLGGCSHPSRHSPHLPPPPPVQFRAGPRGRQGSPSRGSPS\GAFPAGPGGAAAAAVGDDQQQQEQHGAHEGEENNEGNSVPCG/PGKTGGSSVSPGLPEPWPPAPLWTQPSWSAPCH\P*KPPIPPTRQVLGRTGCFLLPAP
3721	34089	A	3761	181	581	ADELNVPLT*APAIPLSKEMKLHVPTKPARKRLKWLHSQQPTCPSTGEPVSNCG\PPPVPQPTTQQYQGLDAGATTRVPRSLLRSEGSQTQKSPSCGSHSQDNSGG/SQSSPVTPQHLLSPRAPQAAPSPDRAPV

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
3722	34090	A	3762	18	2104	RWQGDKRDSA*RGNLRARKPSKRGK/DR*RRVSPTRSGKRRGAEEKNRQEKKKGREKERREKRSERQRDRRRRKEQRKEEQRRRARTNERKPRQTQANGATSS*KASAQQAGMWGGSP*TDATAIRRGGAPCSSRRTCLNQGTIATPSGR\RRHGDAG*PGLASEHDASGHGCLRTGAG*PSDSTESVCRRPLAMHVPTHESHGPVFTRLVSHTFHCG\SKLPAVGRPVACRPTYSPSLCHNPQRPAQLLAHSSALQCAPLSWDPQRCAPPSPRPHRRGPPSPHPHRRAPPSPHPHRRA/HTTARTDPTTSAPPP/RQTQRRATREPATKHTRNAHPRRSACNRGTHTHPRRRRTTERTTHHARPRNRGQATPNTRQPTAGRHEETDGATRRRQHGQTRGEGG/RRRGRAAKTRQRERQEPPHDNTRRTRRRPKRRDRTGAPAGTRNRTSGHKKRQPGTRASTGTAPASQQQQTPTVLSRCISRFGVFYGPDFSGG\NSFCSLPLMSDSTLSTYGGQRRG/RSRARKTQDTGVLSPLRRERSCPPAHGRFPGLFLSTHRQVGPAALRPPELSCE*LPQDGDFCVWLPSLRSRLRGTRVVAPASSP/CGDWQVTAVAP*PQTQSPSLSQSRDVEKRHRGQHPSVGSV*LMKAA*RGPSGAKRPKTAPRPQCRARVLPKRSGPTSPGRGSCGSQSRTRGF*D
3723	34091	A	3763	1	446	MWESLELPRDLLNGFDQNADNDMDNEIQAEVVSDGDEELVGNWSKGKQLKSSENLQLDDATEKKNLFSEEKFKLAEETYLSNEEPNINSQDNGKNVSKACQRTLEQAFPS/SGS/GGLGGKNGFVG*AQSPSAVCSLGTWYP\CPSCCSHG
3724	34092	A	3764	186	529	GTCWKLEQSTLPLLHWAGLACPLAPGTCTSGPLL/TAPQR*MQLCGSPGWHWKRSVVVAPGRQLPGSGECMFQLPLPCRQPSLCAIPPILQANLPLNGRQNCCAQISCKEDQSFH
3725	34093	B	3765	73	1374	
3726	34094	C	3766	1	873	

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3727	34095	A	3767	603	1208	FTTCSKHQTRPGHRPEQQHPAE KSVSGIFCYAEEMESSQLPDPGS GQPPRGG/ALGPPYEPLSNRIPD APG/EAGPASTPGH*SLDQGIPG *PGLAPRGHRLWKSPETPAPSP APRGVSGGLPGSRSAQVGSGDP SPHHL*QPAAAGRKDSSSF*AT WRPP/GPPGPAAAAGRKDSSSF* /GHMASPRPPGPAAAGRKDSSS FMVLP
3728	34096	A	3768	872	1015	VIRSRMLIPKTMGKVSPGHVRG LHSRPSQHRPRGLGGKNGFTAA PAMAEGSNI/GALAVASEGASP KPWQLPCGVEPS/IRRCMETPG* PGRSLLQEQVPHGEP/PARAAQ KGNVGLEPPSTVPTGVPPSGAV RRRPPSSRPQNGRSTDSLHHAP GKATS/SSMPAPESSYEGGGTL QSHRGRAAQDHGNPPLASA*P GDLVKLQLLTPQSDNSCTHIGD NGTYRSQLKAAFAEKLNMGKL TFFITGVNHKWGLPLSLTWLPA NSWESLLSFPPPSPPQQLNDKPG RRSNITHSSKEDKKTEESLELPR DLLNGFDQNADNDMDNEIQAE VVSDGDEELFGNWSKGDSCYV LAKRLVAFCPFPRDLWDFGLER DDLGYLVEEISKQQCIQEVTRV LLKAFSFIRETDHKSSENLQPDN AIENKIAFSKKKFKPVAEICISN KEPNVNPQDNGESVSRACQRSS QQALPAQAQRPRRKKWFHSCS
3729	34097	A	3769	234	636	GPVSGHHRVNCLPCTILPLRR*R AKGHLCRLLCPAGEATGARWR HSPQPLALLQRAPEPAHHHPAA PPGRLHHAGLRCSPVRPAEEGR GPRPQQRARTASLQLLRRR/SLL QPQPPD*\RDKMAEPQRRSRQP AHL
3730	34098	A	3770	1597	1878	DTPRFHSRSKRGITLQEYASSRN *RTSSAVPVF*RMSVRGMEVPC SNER*TQSISGDQVRPAEEGPGP RPQQRARTASLQLPRRRYFLQP QPPD
3731	34099	A	3771	97	471	GVEELRNVNVFFPHFKYSMDT YVFKDSSQKDLLNFTGTLPVM YQA*ICHCWSSSSSSPQVSRGTS HVFSI\TSDEARQVDLLAYIAK\T LKVFQIQIQRAGQIMRIKQSIKL LWLEVENSVLPAH
3732	34100	B	3772	1	1449	

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3733	34101	A	3773	1	927	MQRWFNICKSISVIHHINRVKTYMIISIDAEKAFDKIQHLFMIKTLSKIGIQGTYLHVIKVIYDKPTANIILNGKKVE\AFPLRTGTRQGYPLSQLFFNIALEVLARAIRQ/EEIKGIQISKEKVKLSLFAGDMIFYLENPKDSSKKLLELIKELSKVSRYKINVHKPVALLYTNSDLVENQIKNSTPFTVAAKIIKYLEIYLINYMKDLYKENYKTLLKKIIDNTNKWKHILCLWIGRINLV\KMTILQKAINKLNTIPIKILP*FFTELEKPILKCIQNEKRAHIAKARL/SQKNKSGGIRLPDFKLYYKP
3734	34102	A	3774	1	639	MGRNQSKKAENSKNQNAFSPPKENDSSTAREQNWMENEFDMLTELDFRRSVITNFSKLKEHVLTHHKAAENLEKRLDKWLTRINSVEKTLNYLMELKTTLFMVDNG/CR*LENSHDL*AYFLHLLGNTGL*CCVRGQIGDGKEKREQRDSRSMG/EILRAQLEPFAFHQRSVQCGDIRDLWMGYFLLNLMKKLTFQ*FP*QDT*QLKELKKIAST
3735	34103	A	3775	3	1079	APGPRGAGAQKACGASAGGDPECAAY*GGAQCECGPTVGPGEVPRAV*VWVHGGPWAGGYPVQ*CDAGGREGSFAGAAAAPGGAAGEPAGPCPGAAAAEPAGAGAQQPPAGREVCAGDSGPGAAPEAGGAGGGGAGGTAVPGGDPRAAAGPASGPQGPGTAAAAAGGRARGTAGAAPRPQGQHAGTGAGPPGAAGPARAAAGPAGQRGGTGGGPAGRA*TPDARWASAAGPGGGAAEASERARQGSDAAGRVVSGAG*AAG*TRGATGPAGAAGAGAGTAGDAEPAAARVQPAAGPERLPADHAV*AIDTAAKCPGRGEPAAAG*SSGPEPGEQGAPGAQPGESGPPAPRTAGVPGPA
3736	34104	B	3776	45	149	

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3737	34105	A	3777	3	442	EGKDERND\GKDEGKDEKKNERNDGKDERNDEGKDEGKDERKDERNDEGKDEGNDEGKDD*KDEGKDEGKDEGKDDGKDERKDEGKDEGKDERKDEGKDEGNDEGKDERKDERKDEGKDEGKDEGKDERKDEGKDEGKDEGKD\EGKDEGKDEGKDEGKDERKDEGKDEGKDEGKDEGKDEGKDEGKDERKDEGKDEGKDEGKDEGKDERKDEGKDEGNDEGKDERKDERKDEGKDEGKDEGKDERKDEGKDEGKDEGKDAGKG
3738	34106	A	3778	459	660	VRGHEWAQKKYHKFSLWSVDST*N*QPSPHASGCHWLEEPAAFCHASPAASGIFAAAASDRPLLPSV
3739	34107	A	3779	2	440	RPLSLINIHANFLSKILANSIKQCLNRIIHHDGVRFIFEM*E*FNIHRSINVTYYINRMKNKNMII\DAEKAFDNIQHPFIIKILIKLGIEGT*LNTIKALLMAAAACL\NSCCKDARSSRGGMAEGCRLSASSELWAPMSMGGGLR
3740	34108	A	3780	1	1145	RHPGWPTPAACPTTLRWLKAPVWTPGP/QKMEKEPAARGTPGTGKERLKAGASGFAGGMGPRSVPARKKAQTAPPLQPP/RAAPGPERGAALGRPVAQQVPGARLAGGAAGLGFPAVPRVLPPFPCALSGDRSARERPPGALLRPLPC*GPPT\PVVGGKNDQLKERADSGPDPVAADAVPGEAALQARVP/GALGPAKLSPEGAIVAPA*VRGPGRLHQPGLRPGPRQRSDPRFPGSREPA/GERGRGARRGHRRGRPGGPCDPRRPGTQGEASERGEAAEGEAAEGGET*ER/GGRGKRRGHGPPGSPGKPYPSAGSHAKGATGRGHGTPGTPSPGRSRPGCPRGVPTRSSGLGVARSSAQARGGTEPAPRRSPGAPSGRPATLAK
3741	34109	A	3781	218	376	TRNKILYRQANAERFCHHQACPKG/RS*RKH*TWKGTTGTSHCKNMPNCKDHQG
3742	34110	A	3782	2	187	FTFWHDFAAAGTGCSFPCLVLPSWW*QNLSAFACL*RILFLLHL*SLVWLDMKCWVENSFL

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3743	34111	A	3783	1	220	IALMVSTIWHVFAVAGTGCFFPCLVLPSGALVRQA*W*QNLSAFACL*RILFLLHL*SLVWLDMKFWVENSFL
3744	34112	A	3784	713	997	KFFSLRMLNIGPHSLL/CLQSFCQ\RSAVSLMGFPLW\EPDLSLWLPLTFFPSFQLW*I*QLGFL*LLFLRSIFVAFSVFPEFECWPALLDWGSSPG
3745	34113	B	3785	1	1698	
3746	34114	A	3786	948	1121	
3747	34115	A	3787	1211	2437	LTKRWPGTNTSPESG*SRRAACAGL/LIPFTSRSSSPTWTRPLLS/ACASSHDPGHHNSP*VLVPPDGGTQGFLVLHQADDLHRFLIKILIDIVRQRRENGVKILLGNRVMYHEHSPQVRGGQQLEQLPLITVHGGGLQLLHHVLSEGHSAVQNWGWTLPFIIAKLLMNLH
3748	34116	A	3788	1	1908	
3749	34117	A	3789	1	1788	MTGVSRGSGLPISMAENRRPLPVSAGSKPVIPILQSPLQILNTTHYFLKSLLTPTSSFAHVISSAEDLVQRRNVIGDVYSQGPASPFEINNGLGSPLKYTAWRKQEMGPWQWLWQQDFHLFLGAPLQRYAEPLPVGTISPGWGSCVVDSSQESLPNDKHLRAAKEVPLQLQWQRSFQLPLGASPQRNTRILLTGMFSWVWLNIHPGTLLGEKLGSWGSKGRTTAGAIAERLLVSSESSIPGNPEQLPRNAELPLTEVFRCG*IFIQGPCLVKSWGPGAARAEPLQEP*RRGCWFLLRA/AIPGNPEQLPRNAELPLTEVFRCGQCSYAAGTPQKAPCPVRSSRARDPCRKPSDCLLGTDEQKDSSNLCRLKCPCLTALKRAVFLPARSWRSENGQTASSSGSLSPEQPKWEAPPSRGRLTPHTAGSLRSQCDQREEWVSAMEDEMNEMKREGKFREKRIKRKEQTLQEIWDYVKRPNLCLIGVPESDGENGTKLENTLQDIIQENFPNLARQANIQIQEIQRTPQRYSSRRATPRHIIIRFTKVEMKEKMLRAAREKGWVTHKGKHIRLTADLSAETLQARREWGSIFNILKEKNFQPRISYPAKLSFISEGEIKYFTDKQMLRDFATTRPALKELLKEALNMERNKRYQPLQKHAKM
3750	34118	B	3790	116	885	

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3751	34119	A	3791	593	883	
3752	34120	A	3792	47	716	EAPACL*KALSPLAPTTISSVDCGFRASTGITLLPRTGAAHGAAG*DRGGRAGVLTMTASRACCAGP*SS*RYLRQ*TPNSLEGPTGRSLRSRASPGF/TLRDPVTQPSSPVAAVS/ALGVEPGLAPAL*SQRV*ALPR*TRRKSKATAPTATKPNAGHNTTKKARPGQGPTPEIPALGSPREVDPEVAHPGAFLSQPERRRCVLGSSFPPGYQQRRVDPLPV
3753	34121	A	3793	2	829	GTRAGWRRRRSGRDGPEVTPQPPGAARDGAG*TGPSPPRCAGPA/TAAKPSGHPPPGDFIALGSKGQANESKTASTLLTPAPSGLPSERKRDAAAALSSASALTGLTKRPILSSTPPLSALGRLAEAAVAEKRAISPSIKEPSVVPIEVLPTVLLDEIEAA\SWRATMTGSRACCAGP*SS*RSPAPSLTAPST*ASCTWPRSSPTSSPLRASLRLCVASCGGTPPSTSRPRGTAWCLCWPVTSSWPPTRRTRTGPRSLSRCTSRTPWGSGSGWTALT
3754	34122	A	3794	114	254	
3755	34123	B	3795	1	2052	
3756	34124	A	3796	860	1090	
3757	34125	A	3797	2252	2557	LNPLSMGRRWPGEETVTDPGWKRLCHPLHWVAETVPVQAVGAPWSLQMGGWNWGGRCPQHLAPSKGVM*RLPGQFGRTPSWKEVPEVWGMFRRPACGPRLS
3758	34126	A	3798	444	854	VSHLEAQK*PSWTC*HQCQWALPMFPHHSEADGLIE*WNGLLKSQLQCPPGGNIL*G*GKVLQESVYAQNRHLIYGTVSPISRTHRPLCSQSTQDSCLLVANPSQICLVHIPFP*VQHSLGL*ISWDWTGEVGPFL
3759	34127	A	3799	1169	1881	LEHPATVIFCFSWETFDPQGFCFSLPKVSGTCLISLLLHAFPFVVTSAPCPQEFPHSPHLCFHVP\HHSEADGLIE*WNGLLKSQLQCPPGGNIL*G*GKVLQESVYAQNRHLIYGTVSPISRTH\GHQVTHGQPVKTT/LL*SPSMGSWGIALVLPPL\DLLLSG*SLTLPLAFLLRTHPLLTTVQRRAELPFTSWICFLSLFERGKGPGQPLVTWTECQALTLLPSPGSHTQGTWRIPH
3760	34128	B	3800	65	1324	

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3761	34129	C	3801	1	1263	
3762	34130	A	3802	1	2845	MAPRSLRMEDAIESLAVVSSEYVGAGVNWMFLPPSSKSTCKILTPHVMVLGEQGLAPPTVFLKALPIPLYHTVPPGGLQPRAPLVTGSLDGGNVPFILSPVLQPEGPGPTQVGKPAAPTLTVNIVGTLPVLSPGLGPTLGSPGKVRNAGKYLCPHCGRDCLKPSVLEKHIRSHTGERPFPCATCGIAFKTQSNLYKHRRTQTHLNNSRLSSESEGAGGGLLEEGDKAGEPPRPEGRGESRCQGMHEGASERPLSP
3763	34131	A	3803	1	279	
3764	34132	A	3804	2	517	KGLAFEVSLADLQNDEVAFRKFKLITEDVQGKNCLTNFYGMGLTCDKICSMVEKWSTMTEAHVDVKTTDGYFFHLFCVGFTKKHNNQILKTSYAQHQQS/RQIQKKMMEIMT*EVQTNDLKEVVNKLIPDNIGKDTEKV/CPIYPLHDVFIRKVKMLENPGFER\MELRGGGS
3765	34133	A	3805	18	602	PAPWRLACNKRLTKGGKKGAKKKG\VNPFSKKEWY\D\VKAPAMFNIRNIGKTLVTRTQGTKIASDGLKGRVFEVSLADLQNDEVAFRK\FKLIT\EDVQGKNCLTNFHGMDLTR\DKMCSMVKK\WQTMIEAHVDVKTT\DGYLLRLFCVGFTKKRNNQIRKTSYAQHQQ\VRQIRKKMMEIM\TREV\QTNDLKEVVNKL
3766	34134	A	3806	525	1173	GEPHSQATSGHFASSAGDTQANRVWSGPPANTNRPAAEGHDC*KEN*ETERTSTPKPHLYVTIIKDQRKGISD*RSNE*NEARREV*RKKSKKK*TKPPRNMGLCEKTKSTSDWCT*K*RGEWNQVGKHSSGYYPGERPQPRKAGQHSNSGNTENATKILLKKTNSKTHNCQIHQS*NEGKNVKGSQRERSGYPQREAHQTNR*SLGRNSTSQKRV

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3767	34135	A	3807	111	1329	RNRRRERHKEREGGGTGGTDW *RRGNRRKRTQRGRDDERRGR DDDQNHTTNTRRETTKTKRTT NRTQQKREQKRNETSKRNETK RATEQNRRERTGTRSGRSAKRQ RTEPERERAARRARAKRTASAA RDRGLSSTFQLPTRSGNSVHTS KKPLSRKYEQDPWADS/GSEGV WKPVPRRLEAKVMRESQGSSR SCCNSRTSARLITRTMR*ATLSS NKWSFCMPAGRCLTVTSPCCTP CALVTRKMLVTLGL*SRSRELT T*GTFVRGKQK\SVFSAAWGPG HQAQCSEQPSRGRFHRAQPMA *EPCCKSRHPRATPLHPRPSRPK SPTTPPPTRQNANNKGHNTTHT KPRAPPEPQTTQHEHTPQPPPDS HAQDNNNKNTPQQPPTKNAER PPRPTAHPPPAHKPLL
3768	34136	A	3808	2	517	
3769	34137	B	3809	1	1008	
3770	34138	A	3810	139	1407	WRGGLDSALRAAVTLQGCAGC DRPGSA*SNNYSI*I*R*RW*SN YSEK**GNEGNAVILLFHSNGT ASKWTVNRASADISKSLQASW GTEHTWPEGEYS\AGPSQHSSP AVSDSLPSNSLKKSSAELKKILA NGQMNEQDIRYRDTLGHGNGG TVYKAYHVPSGKILAVKVILLD ITLELQKQIMSELEILYKCDSSYI IGFYGAFFVENRISICTEFMDGG SLDVYRKMPEHVLGRIAVAVV KGLTYLWSLKILHRDVKPSNM LVNTRGQVKLCDFGVSTQLVN SIAKTYVGTNAYMAPERISGEQ YGIHSDVWSLGISFMELALGRF PYPQIQKNQGSLMPLQLLQCIV DEDSPVLPVGEFSEPFVHFITQC MRKQPKERPAPEELMGHPFIVQ FNDGNAAVVSMWVCRALEER
3771	34139	B	3811	1	1134	
3772	34140	A	3812	374	931	WRGGLDSALRAAVTLQGCAGC DRPGSA*SNNYSI*I*R*RW*SN YSEK**GNEGNAVILLFHSNGT ASKWTVNRASADISKSLQASW GTEHTWPEGEYS\AGPSQHSSP AVSDSLPSNSLKKSSAELKKILA NGQMNEQDIRYRDTLGHGNGG TVYKAYLCPEWENIICKGHTTR YYTGTSEANYV
3773	34141	A	3813	3	444	

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3774	34142	A	3814	75	807	GIAGFVNIHLDSLSFLTGVPGVKAERF\E*RMTAKHCALSLVGEPIMYPEINRFLKLLHQCKISSFLVTNAQFPAEIRNLEPVTQLYVRVDASTKDSLKKIDRPLFKDFWQRFLDSVKALAVKYLQRIGSRTPMDTKIYSYCPAVHPAEPTDMKSWPSLFEVPTSLEYCPFYLQLVESADAEGTQKYRRLTAYYIPVYTEPPLITKEPSCLWKQAEFGDLGKHVWLVEQFSSTRVQEHGVGW
3775	34143	A	3815	35	2088	KVMNKRSQTQNGTRYMTPPPRSSHTKQHLL\PTPPPRSSHTKQHPLHDPITTKLTHRT/CTRYTTPSPRSSDTEQHPL\PAPSPRSSDTEQHPL\PAPSSRSSDTEQHPLHDPTTTKLTYRTAPATRPHHHEAHTQNSTRYTTPSPRSSDTEQHPLHGPITTKLTHRTAPATRPHHHEAHTQNSTRYTAPPPRSSDTEQHPLHGPTTTKLRHTTAPATRPHHHEAHTQNSTRYTAPSPRSSDTEQHPLHGPITTKLTHRTAPAT/PAPSPRSSHTEQHPL\PAPPPRSSDTEQHPLHGPTTTKLTHRTAPATRPHHHEAHTQNSTRYTAPPPRSSDTEQHPL\PAPPPRSSHTEQHPL\PAPSPRSSHTEQHPL\PAPSPRSSHTEQHPLHGPITTKL/STQNSTRYTAPSPRSSDTEQHPL\PTPSPRSSHTEQHPL\PTPSPRSSHTEQHPLHGPITMKLTHRTAPATRPHHHEAHTQNSTRYTAPSPRSSHTEQHPL\PAPSPRSSHTEQHPL\PAPSPRSSHTEQHPLHGPITTKLTHRTAPAP/PTPSPRSSDTEQHPLHGPITTKLRHRTAPATRPHHHEVQEQAKPIK*PPRPSPETTRAQPREPAVTLLPSGALGQACPCDATAGPHGTTLWPAVPPRWQQHLTRELLHPVPRACP*QGQGQPFTAGPGRGSHPYDPTGASPKGQSSIL
3776	34144	A	3816	83	184	RLTLPDRLGSPPDTH*AQHITRAVLPQGFTDSPH

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3777	34145	A	3817	1	811	MAEEDSGNLQPEGEGEAGTSS HGGAGERVKGKVLQTFKQPDL TKQTRFIRGPKTPAPVTDWEGS LPLVFNHCRDASLIIHPHFKGVR PRRDACLGPSPLAASPAFLGKG QHALKRLKPIITRLLQHGLLKPI NSPYNSPILPVLKPDKPYKLVQ DLCLINHIVLLPIHPMVPNPYTL LSSIPASTTHYSVLDLKHAFFTIP LHPSSQPLFAFTWTDPDTHQAQ QIT*AVQPQSFTDSPHYLNQAQI SSSSVTYLGIILHENTRALPADH
3778	34146	A	3818	2	324	HFEARRQAGPPKPSPQPPFR*LP TAGT/RGGGGEKAAGGFRWGR FAG/MGQGPDPPGAHGQNPASP SLDFPWGPICASQGVTDQSPSTF QGPLGEA*KPTAGAKPGAGAG
3779	34147	B	3819	206	1391	
3780	34148	A	3820	229	792	LGSSAGNSAPDPWRPTSSGVFS FHNTSHSHWILRLRTQERFSEV CVQGTWPTRPLWALPPP*FPFPS PAPAAFASCQSLPPHSPQSPRPG AGIS/RPRSQEAPDSSQ/PAPTRP SVPSPMANQGSGDDRQPPPPQD TPPRPNAASQSAGHNYASLPAP RGRVGVGIGFPGSPACAGGGIW HFHTLSFPAF

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3781	34149	A	3821	3	1676	KDNERRLNTCRSTRSHKRAHTRRSIRAHRGSAAAPPAAQAPGWRWASSCPRVQSAAGRGGRSGAASGR*APRWGCPP*CGSRPGKCSPSPAPLASTFPRPGTEPPCRL*RGTCLGSACSGGSGRG*RR*GTGTQRRCPLPSARPRTRRRQISCQGKFS*CPSASSTNVCSPTGRGL*KPVPWAPGGRRRRPS*GRSSGDLSSGTWWP*S**ELGIPEYSHST/QG/LVGVAMPPHRRAVTGNVHIAGQARKKDSP/GGRSPAWL*SPLFCAPGGRGASHLLLSFP*ESPAP*TARP/PLPARKLTVPVVLLRDGLGRGGLGRR*PCSAEKS\GRGRSGWRRARRPPSEAGTRGNRTSSSWRAPWRPGLGTGEPPGAPPGFAPSSSPRRTPISPLSPASGSGGSGLGRRQRAADRARTKPGGD*VGSWAGRRPPGGAEGP*GQRRPRPYAVLLLSGWP\GGEGGGSLQPSVQLLVQGGPVGLTG*VSPRLLTREALKQNGATEAGGEHWPSCPPSH*/PGAGEHPGAADTLQVASPA*GHGTAGRQGRAPAAHPAHRGQRAHSTRQ
3782	34150	C	3822	78	371	
3783	34151	C	3823	349	591	
3784	34152	A	3824	822	2114	AGRSVRIQAMTCLHPAHLGYPGSFQAPESSCPGQ*GRMHSQPTP/AGRRDMQDEPSFSNNIGVAGPGAMSRYTCPGCKNSNQRTEEPKKMR*TF*SLSSFPWGSGSPHPVPSFLWVPPSQLPNT*KLRAGLGTSGLAPGGTQKLRFMRASLWQSKKSRLCPRWGPSGPVGSV*GVEGVAE*RQGLGT\AGSGHQPERTGHRLWPAASG*SLACSAPSRKGSCFSRPSLRSTETSLPAPGSLSAVGH*GVESAWPAAGRAGNHFGPEVADNLYEMKPPEPQVKPGLGRRQRAADRARTKPGGD*VGSWAGRRPPGGAEGP*GQ\GGPGLTLSFFFQGGQSGEGGGS/PAAECISGGDSDVALQGSHCVHSEQGCLAELEDPG*EPGVAVPGWGSQERNVAGTGGVSAHGDTACRPAPPGHW*PTGRGDEIVEAKTK

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3785	34153	A	3825	3	452	PRHSPGCRCPVAEGQSSGRALPPRLILLAVLLLLLCGVT/CWLCPVLLPPEAGTGPATSATSTAALRCGSHPYGQ*QPCTQ\P\GPPTAPCSTHWACGCPAFGSWNWTPW/PPPAYSLYTPEPPTSYDEAVKMAKPREEGPALSQKPSPLLGAS
3786	34154	A	3826	16	118	
3787	34155	A	3827	292	1047	SWQELESRAQAPNVGQRDGPRRGLSYHVAAEVNELLVEGQHRLEGDKHFTGHSG*QGARGVKAAGRDP*\PRGLVKAVGRGAMESRSSSPKGRGNRMPSGYCTEL*AAGNQSGFVEAGLAFTPAIST\PTGGPLGTHRSQCCVQGCHCP*G*LPRRRAAVLVADVAGPVPASGGSRTG/AQPAVTP\QAEAGGPPAG*APLATGCSSGPRAGTGPRGRSCRPRSPAPPAAAAGAAGAAGAAAAAAVRGRSAAPGP
3788	34156	A	3828	2	462	GPVSIGEPEIGPPGPVSIGEPE*GPPGPVSIGEPEEGPPGPVGIGEPEEGPPGPVSIGEP*EGPP\GPVSITEPE*GPPGPVSIGEPEEGPPGPVGIGEPEEGPPGPVGIGEPEEGPPGPVSIGEPEEGPTGPVSITEPEEGPPGPVGNEMSSR
3789	34157	A	3829	3	374	YRALVFSSSTQ*VSKNFLYSGSSSMLPVLASFFLSFFLAIFWNGANSATAGYSRPQVGGEELEVVVCWQRAQLLLQLLLGEARRQAADDHLRGARGRSHRGGAWTRSSKGTAYRAGRPGPRPTK
3790	34158	A	3830	66	619	VRSLFSEMNVVEFQNGFWNMFPVKRPKISCSGRVCSIPEDSQKEAEKKRCQDWKHRR*SRI*EVFRNL\RVEEEKTSANPETLLGEMEAKTRELIARRTTPLLEYIKNRKLEKQRIREEKREERRRRELEKKRLREEEKRRISVEDRWLYTIRINRRKSQRKK*GLRSHSGSDKEHRDVERSQEQ
3791	34159	A	3831	253	482	QVSTCYHSQEKEKKRISSTSKSLNKEKRRNEQ\KDQ*ALLSSPPSPPAESQGWHWSSLPPHSRFLKTSYILDLDIKK
3792	34160	A	3832	156	443	
3793	34161	B	3833	426	513	
3794	34162	B	3834	47	1311	

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3795	34163	A	3835	1503	1652	NCGNNQ*LTNQKKSRSRWIHSQILPDVQGGAGTIPSETIPINRKRGNPP
3796	34164	A	3836	1	1986	
3797	34165	A	3837	1	1116	
3798	34166	A	3838	1	546	ERSSSPAAEQSWMENDFDELREEGFRRSNFSELKEEVRTHGKEVKNLEKRLDKWLTRITNTQKSLKDLMELKTTARELHDECTSLTNQFDQLEERLISNFSKVSGYKIN\GKNHKHSYTPITDKQRAKS*VNSHSQLLQRE/YKYLGIQ/AYNGCEGPLQGKLQTTAQGNKRIQTNGRTFHAHG
3799	34167	A	3839	1	987	
3800	34168	B	3840	1	1593	
3801	34169	C	3841	1	1479	
3802	34170	A	3842	129	368	
3803	34171	B	3843	1	1884	
3804	34172	B	3844	1	471	
3805	34173	B	3845	1	675	
3806	34174	A	3846	1	410	
3807	34175	A	3847	250	880	GEVTKPQFAQFFHGSLASLTIRPGKMESQKVISCLQACKEGLDINSLESLGQGIKYHFNPSQSILVMEGDDIGNINRALQKVFYINSRQFPTAGVRRLKVSSKVQCFGEDVCISIPEVDAYVMVLQAIEPRITLRGTDHFWRPAAQFESARGVTLFPDIKIVSTFAKTEAPG\A*KPQVQNSEFSL*AFENPVSCQISNSGHVPNFQFRV
3808	34176	A	3848	890	4889	
3809	34177	A	3849	1	799	MYAQPPNCKREKASGDVSLYWWKLAKGCLQMEVSEGAPNSASTPTGNTVSQELNRPLP\QPPYPRRFSWVCRSSLQA*VAESATKTSAFRAPNSFCRLQPRPCCRASPASPATSCTCPGSLAWARPAPASHWARPHRPPPCPTSPRP\PRGRDAPER*AHGPPVPDAR*GALAPQATGGGQPPGAQPHHARAGPGQPRTPL/Q*GLCARPGEPQLRVTPHGPQAGG/HTQRLPPMGKPGVSGGVCPHSDFPQPMPTVEMTGPRSGVQRPT*DGTGWLAPDAESLVSFEFSSPT*VL*QQWK*RSGVQRPT
3810	34178	A	3850	212	361	

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3811	34179	A	3851	3	909	GGRQRGKDTGHMAKQEQERE VGGATHL*TTRFRSCSK\SALIP VIPITKSTGSRFRNSVEGLNQEIE IIIKETGEKEEQLIPQDIPDGHRA PPPLVQRSSSTRSIDTQTPGGAD RGSNNSSRSQSVSPTSFLTISNE GSEESPCSADDLLVDPRDKENG NNSPLPKYATSPKPNNSYMFKR EPPEGCERVKVFEECSPKQLHEI PAFYCPDKNKVNFIPKSGSAFC LVSILKPLLPTPDLTLKGSGHSL TVTTGMTTTLLQPIAVASLSTN T\SKTESLEEQVQSCHQLLYSHH QNQLRKLKD
3812	34180	A	3852	189	454	LWKRFNSWTSLRHPYQPYQAE QIAPQTCGSQSDGGLPSSSGPAP LHHAGLGYGTEGSPGARRRVE GQDP*VLEQAAGPTPPRYLVRP
3813	34181	A	3853	17	561	IPGSWRQKMPVPPAA\PAHAQG RPGALQSPGSSTPAQPGSRWEV GGPAAPWGSLRHP*QPYQAEQI APQTCGLQSDGGLPSSSGPAPL HHGGLGYGTGGSPGA/LEEGGR PRSLGPGAGSRAHAAEVSFPSG PPSRGLTGSGFCACSEERAGFPR ELMVIKNTVTPTREATTLILTKA PAILP
3814	34182	A	3854	1	540	FFQPIFWGKDPQSGTPPHP/RPG PAPSGPEPSISMVTRRWLRAPN CSDRRGEGPRTEADRHGSCCRF RSRAGTAVHSCRRRHPRAAGLP SSLCAEAGPRET**LEGGCREG AEPRP*RPGSGAHAHTDPERAH RSGARTQ/HPERAHRSGARTQIR SAHTDPERAHRSGAR\HRSGAR RTLPL

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3815	34183	A	3855	1326	2409	GRPPGVPPATAPRAAPGAGDGEAGTPAPGDHPEPVCRIQPG*WGT*GWGASQHWGGH\PALALAGRRPSRGLAGASGRSSEEPGVATQRLWESMERSDEENLKEECSSTESTQQEVLALEEERAQVLGHVEQLKVRVKELEQQLQESAREAEMERALLQGEREAERALLQKEQKAVDQLQEKLVALETGIQKERDKDLQRQCCGMMGDRAKASPSWTSTVILKFPLIKNCLNPKDISLMAKELWSLRTMDALNRNQIGPGCQTQTMVQKGPLDLIETGKGLKVQTDKPHLVSLGSGRLSTAITLLPLEEDCLPSLVDDLVPRLGLKISLETRRRGQLMLCTPKFENQWPTTDKMPETSTGSH
3816	34184	A	3856	240	639	DHGRSQ*EPNRPWMPDPDHGAERTLGPDRDRQRAE\MQTDKPHLVSLGSGRLSTAITLLPLEEGRTVIGSAARDISLQGPGLAPEHCYIENLRGTLTLYPCGNACTIDGLPVRQPTRLTQGLSMSLPSQLIQET
3817	34185	A	3857	1	1758	MALLPTVLCLWAQAQVGVQRHNHIFWNEKEHGHGKSGSCHNGASCSAEDGACHCTPGWTGLFCTQRKPHLLASQPLRIPCCGLLATVGIVQTSREGGMQAAPGLVVPDSCPTRTEELCRGSSRPDWIQGIDKPKVLQGCPAAFFGKDCGRVCQCQNGASCDHISGKCTCRTGFTGQHCEQRCAPGTFGYGCQQLCECMNNSTCDHVTGTCYCSPGFKGIRCDQGIMLLLFLIV/CAAGPICLASAAAEREGPRPGSPCLLHTCHE/R*PAPTTPSQDLTDHYLRFSMPIMVLT/CLQGAFPGSPGR\PG*TWAPLCGMNVNRPGT/HELGCDSDHWGPHCSNRCQCQNGALCNPITGACVCAAGFRGWRCEELCAPGTHGKGCQLPCQCRHGASCDPRAGECLCAPGYTGVYCHPVTGACTCQPGWSGHHCNESCPVGYYGDGCQLPCTCQNGADCHSITGGCTCAPGFMGEVCAVSCAAGTYGPNCSSICSCNNGGTCSPIDGSCTCKEGNVPSLPSPSLTYEHIPQVVLPAEGSQDGTFGLNCSEHCDCSHADGCDPVTGHCCCLAGWTDIQEGFLEKEGPKR
3818	34186	A	3858	2	2414	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
3819	34187	A	3859	1	852	DEEEVVAREEEEEEEEEEMVPE ESMASAGPEDFEQDGEEAALA RGAPAVDSLGMEEEVDIETEPV AHEKRPSMLDEPPLPVGVEEPA DSREPPEEPGLSQEGAMLLSPEP PAKGLAHPNGSQKVIFRVPLRV IHGPKAVELQVFPGLHKQPTNQ PK/TEPCDPHSWFKSCYHLLFIP VGISRPP/HNPTITATIFASTASV LW/PVLDTCMSSNSGYFKAVLE SYSSKVLSVTQYGNPRATGSAG LRGRPGS\PGSSGSRGPAWP*PQ AAPRCPPSSGRPGPTSQSPS
3820	34188	A	3860	3	1997	AQGSVVPGLFWAFLQLEVNCL LESPIIQGKFHFRLERISVVEPQE RKRLSFRKSEI*P*K*SLVKKL*E RLKTRKQMQLANRLRRYGYSV VES*FPNLKVSSSVSTTPTTTYIP MTHKAIFSSYFLWDGRSAFLTI YKMMSSHPQEEEEEEEEEGGE GEERKRRKKEEERGKRRKRRR RMK*RRRRTRKRRKRRKMK*R RRRRRRNMRKKRKEGKNMKK KM/REEIKRQNALYEIEMRKKL EKKREEMHESRRRFLAPLFSSP TANCSTSLVPRLRLASLPAALPS NRVVRVTTPPAGVRGAWRHSH FSRSRSIMDTSSEMLVRFGRRC GRAKESTGRDWNSLKSSEEDR KMWESLELPRDLLNAFDQNAD SDMDNKMQAEMVSDGDEELS GNWSKGDSCYVLAKRLASFYL CPRDLWNFEKDDLGYLAEEISK QQSIQEAQRSRRKKWFYGPGPG SLCCVQPIDLVPCVPAAPAMAE RGQCRAHAVASEGGSPKPWQL PHGVEPVGAQKSRIEVWEPPPR FQKMYGNAWMSRQKFAAEAG PHGEPLLGQCRRELWGRSSHVE SLMGHYLVELLSIGAMGIKVQR PRCFFDIAINNQPGEKGTGKSTQ KPLHYKSCLFHRVVKDFMVQG GDFSEGNGRGGESIYGGFFEGP AMGPNATNNFTKLAG

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3821	34189	A	3861	86	1120	LVLSKGKEHLLGIKEHEEEEERRKKYE*KDAEEIKRQNALYEIEMRIKLEKKREEMHESRRRFLEHMQDKHIIKAVEQQQ\RQRKKMKR*ENSSKQKKRLIQMGKEKEAETHRLMEKRRERIHNFLSELLKEKLDNEDMIIARDIAEAEAEWEKREREKDEKNQAELKTIAEYRAIVMKNKEEEERQRKIEAKEQLLAVMKADQIFWEHEKEKKCKADKEHQEVQDAHIQQMAKNKFNAKQAKQAELDYCRLTEALVAEKEKEFQDYAREVIELESETPNKYIYPLVKAVQEGPGGGRGPVFVDRGGLRPSYQANDVTGVQLPFYNSQGPKYNFQKSKRRLGFTW
3822	34190	A	3862	591	2805	WVHQPAGS*GEKPT*ISAPPWPEAPTSELWVLTPPEAVQEAAARVGQEVPAAP/RGPLPSSATGAKSLGQGSPTPSTRSMSLQSCAGPQHP*TLRRGPLWGTSRWKMVLT*ASRTSSTPGLT/QGPRVTVLLGKAGMGKTTLAHRLCQKWAEGHLNCFQALFLFEFRQLNLITRFLTPSELLFDLYLSPESDHDTVFQYLEKNADQVLLIFDGLDEALQPMGPDGPGPVLTLFSHLCNGTLLPGCRVMATSRPGKLPACLPAEAAMVHMLGFDGPRVEEYVNHFFSAQPSREGALVELQTNGRLRSLCAVPALCQVACLCLHHLLPDHAPGQSVALLPNM/YSALYADGARPQPPWALAHLV/LYWTWGRWP*GAWRQGRLSSMQKILLHP**LLGPLTAC*LPSASAQALGTS/ETGYAFTHLSLQEFLAALHLMASPKVNKDTLTQYVTLHSRWVQRTKARLGLSDHLPTFLAGLASCTCRPFLSHLAQGNEDCVGAKQAAVVQVLKKLATRKLTGPKVVELCHCVDETQEPELASLTAQSLPYQLPFHNFPLTCTDLATLTNILEHREAPIHLDFDGCPLEPHCPEALVGCGQIENLSFKSRKCGDAFAEALSRSLPTMGRLQMLGLAGSKITARGISHLVKALPLCPQLKEVSFRDNQLSDQVVLNIVEVLPHLPRLRKLEQGRSGAPGVGDSTPD
3823	34191	A	3863	1	2784	

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3824	34192	A	3864	727	1715	YLSKGLKEVREGSLQIPGEIIPGRKKLMQMLSEKTL*SQHHY*KGFLQRQIHQKMIAHLVEQRNKDCMFLQIMPAATS*/TEIQATIRDYYKHLYANELENPEEMDKFLDTYTLQRLNQEEVESLNRPITGSEVEAIINSLPTKKSPGPDGLTAEFYQRYKEEL/PKPCRDTTKK\ENFRPISLMNIDAKILNKILANRIQQHIKKLIHHDQVGFIPGMQGWFNICKSINVIQHINRTKDKNHVIFSIDAEKAFDKIQQPFMLKTLNKL\GIKYPGIQLTRDVKDLFKENYKPLLSKIKEDTKKWKTILCSWVGRINIVKMAILPKAPLPLPP
3825	34193	B	3865	1	1908	
3826	34194	B	3866	609	1658	
3827	34195	B	3867	61	234	
3828	34196	A	3868	1	978	LFTDDLCQPVEATSGQAMVQSRGATTHGGGRGGSCKLLGDRGQGSTSQVGRWGSSCHPPTGG\PARSPCWPTARKPLRGVLQGASLGSTASMLGAASGTPRPPPSWLVSVPSPRAPCWGVPGAG\EQGGPETQPPGAREYPQPAGREGRPQILRFPKSSSSQCLVEFCSLASSCFALEAMKTRRSPSS/SGSSGSDG/SQRTTRSGPAQRPRVSGSSEQG\DGMRGGSSGGMKGRRVPKREPRTEAASSSTA*RQPPPPPSPLPHARRHFRFRPCCGPARDAAPSRAQTEAPPPLRTQSALSWPLCSRTDGKLSRGQSRDGSRAPTPGVL

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3829	34197	A	3869	1	1919	TPVSDEEEGSLHHTTWRNLRIG VRIACPAGENAQSSESPVRACQ PGTKTQYGLNQAWSPGVRRDL IQGSAERPARYPAPGEMGVGAF IPLGHDKRRAASQHLHVSGREG PEALGSRGSALRKQVPAWLPHS LRTCPVDRNPQAPCARTGLMV ETPHHEQWVRGEHYRYKFSRP GGRHAAEGKWWVRKRIGAYFP PLSLEELRPYFRDPHTLMLGQR VTERELDGEPRGPVTVEGRSAT TSGYPTKVTKIGGPLDPAGGLE GPLHGALGSDPLEVSDCPGPHL SRKVWENGSFGASDQQHTR/YT TDGSSWPTVAEKKAPSSKQYH SSMET*R*TGHSNHPRNRPTCG QVPPNENNTRNRPTHTARYLPT /ENNPRNHSTHATRYLLTTTTTE IIPHAARYRPTRTTRYLPTRTTR YLPTKMTREIVPHAATYLPMRT TREIIPHTATY/ASNENNQYLPM RTTSQVPSNEDNPGCLPTRTTR HLPTRTTRYLPTRMTQEIVPHV AWYLPTKALRPFNGKRTAFSA NAAKRSEAPTLR*ALRT*CPVN PPDTEGTGPAMPSLECPEQGNP QRRWAGRRRSSGAQDAGQGTR FTPSLWRAWGWSRLRPRLSAP GCWLTRKCRTEPPVVPQALMM AAVTDMQTLIH
3830	34198	A	3870	295	457	
3831	34199	A	3871	296	1057	GNEVKMPARETTPHRVPTGAQ PSEAGEKGHHPPDRRMVDPLTL ALCTWKSCRHSMPDCKAAGRE AVPCKVTGAERPRPRAPTSA*P SGKLEGLSLWCTQSCSCMLHR AGVISVFFTMEDVAPTRGLLH* RAAIGIISPITISVTKTSNNCRWC RVGGCAN*LRGALEAGG/WLQ NQKGRDAFNKRLRGGMDKPG AGGTCGSGRRNRPLRDRS/VPE VKGGTGTG*KTGSGGLKRKYV GDGTTASFESLRVLIKWPL

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3832	34200	A	3872	3	913	GGADSGERLGPHALGLGAGSGGGRGRYGPSRSRPSGRAADPGGVRPFPVAPRGARARRGGRVVPAF*RPAGAA*AAQHHVVVSEPAAAARGGGGPGGQGSRAWRGVRRLPGGAGGLAGPPGRVPVLGPPGSGPAAQRPPGRGQGAGQEPPPAGDAAAA/PSSGSASCR/GPGAA/GPRALCPGPAPPARRGPRAGLGRPAADRGAPAAAPVRAEPHGLGGAAGARPPHRLRGGAGH/SGALVVLLTLWITGGGGDGDRASPGSPGPLAT/GAGLVGNKAAPS*RAARAPGGLGCRWARFSLTSQCPCPQL
3833	34201	A	3873	2	484	TPWRRKSTE*PTLGVRRPVPRNAMPHHCSFFTGRTVPSMATPGYNEGWDKFRMKCHLCVNYIEMQTDPANCDYVIVSGAQRKEERWDMADNEQVLTTEHEKKQKLETDAMFRLEHGEADRSTLKKALAHT\DHIQEAQSAWKDDFALNSMLRRRFRVPSKP
3834	34202	A	3874	3	531	GRKRSKRMEKGERGEPYSLSLRNHQGSWEPEHMS*KPEGG\VLAFKGDDGFSVWESNAIATYVSNEELWGSAPEAAAQAVQWVNFADDSQYQGVPTLGKMHHDKQATQDAGEEV/QPQFQAVLG\EMKLCENMAHFDAKIFAESQPKKDTPRKEKGSREEKQKPQAERKEEKKVATPAP

SEQ ID NO:	SEQ ID NO: of peptide sequence	Met hod	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
3835	34203	A	3875	2	1326	TMAAGTLYTYPENWRAFKALI AAQYSGAQVRVLSAPPHFHFG QTNRTPEFLRKFPAGKVPAFEG DDGFCVFESNAIAYYVSNEELR GSTPEAAAQ\VVQWVSFADSDI VPPASTWVFPTLGIMHH\NKQA TENAKEEVRRILGLLDAYLKTR TFLVGERVTLADITVVCTLLWL YKQVLEPSFRQAFPNTT\RWFL TCINQPQFRA\VLGEVKLCEKM AQFDAKKFAETQPKKGTPRKE KGSREEKQKPQAERKEEKK\AA APAPEEEMDECEQALAA\EPKA KDPFAHLPKSTFVLDEFKRKYS NEDTLSVALP\YFWEHFDKDG WSL\WYSEYRFPEE\LTQPFMSC NLITGMLQRLDKLRKNAFASVI LFGTNNSSSISGVWVFRGQELA FPLSPDWQVDYESYTWRKLDP GREETQTLVREYFSWEGAFQH VGKAFNHGKIFK
3836	34204	C	3876	58	222	
3837	34205	A	3877	6	153	
3838	34206	A	3878	2	889	CPPWELILDQFRKSLGISPANTG PLCPAPPSCMYPPSPQMPAKAP/ PDHPPEGRPGTTPEPFPRVTCVT E/PVGKGLSRDSQ*ETRGDLQE* SLAAPKSAPCFTHSAICPGAPSM SRHPERSVFLLFQAPVQEPPAPG PP*WVLREPDFGTGVFPEPSW* KAADFEPLGLCPGRSLSAQCPS WWPPTSSDPG*ALLKSGTGTPT VAPRQPAPAAPRFQRPPQPRGL ASTCPAGPQQKGSDPPGRSAGS E/GSVSGKSLKPCLSSPLIPPPQS STQKKASVAKFVEFSPYTKQKS QLSVP
3839	34207	A	3879	1	391	MAKAVEKPESTLEATKSKESV MSRVEWIGTAHMWVDDETGD NASKTQQTLEPAELATKYANFS EGACKPGYASALMTAIFPRF\C KPIRLSP*PRHLAHWCKKWAPK ILGSSAPVALQGAAPVAALMG WR
3840	34208	A	3880	1	346	
3841	34209	A	3881	249	474	VYLLIVLAVLYTNNRQTESQIM SELPFTIASKRIKYLGIQL\TRDV KDLFKDNYIPLLKEI*EDTSKW KSIPCSWI
3842	34210	A	3882	25	302	
3843	34211	A	3883	1	2235	

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3844	34212	A	3884	1	2724	MGGMVESSRHNWSGLDKQSDIQNLNEERILALQLCGWIKKGTDVDVGPFLNSLVQEGEWERAAAVALFNLDIRRAIQILNEGASSEKGDLNLNVVAMALSGYTDEKNSLWREMCSTLRLQLNNPYLCVMFAFLTSETGSYDGVLYENKVAVRDRVAFACKFLSDTQLNRYIEKLTNEMKEAGNLEGILLTGLTKDGVDLMESYVDRTGDVQTASYCMLQGSPLDVLKDERVQYWIENYRNLLDAWRFWHKRAEFDIHRSKLDPSSKPLAQVFVSCNFCGKSISYSCSAVPHQGRGFSQYGVSGSPTKSKVTSCPGCRKPLPRCALCLINMGTPVSSCPDRSTRQKVNKDIQELNSALHQADLIDIYRTLHPKSTAYTFFSAPHHTFSKIDHIVGSKALLSKCKRTEIITNCLSDHSAIKLELRIKTFTPNRSTTWKLNNVLLNDYWVHNEMKAEIKMFFETNENKDTTYQNLWDTFKAVFRGKFIALNAHEKIQTTIREYHKHLYANKLENLEEMDKFLDTYTLPRLNQEEVESLNRPITGSEIEAILNSLPTKKSPGPDGFTAELYQRYKEELVPFLLKLFQSIEKEGILPNSFYEASIILIPKTGRDTTKKENFRPISLMNIDAKILNKILANQIQQHIKKLIHHDQVGFIPGMQGWFNIRKSINVIQHINRTKDKNHMIISIDAEKAFDKIQQPFMLKTLNK
3845	34213	B	3885	1	1971	
3846	34214	A	3886	1	1146	METRPSRGPLTPHTARCQSETKLPEEGSGSNICCSAIFAILQPPLVIPRQTGSGVDLQQTPTDLELRDLTVRRKTNKWKGIASTSTKRTSTPKRHLSWFFEKINKIDRPLAKLIKKKREKNQIDTIKNDKGDITTNPTEIQTTIREYYKHLYANKLENLEEMDKFLDTYTLTRLNQEEVESLNIPITVSEIEAIIKSLPTKKSPGPDGFTAEFYQ\ASIILNGQKLEEFPLKTGTRQGCPLSPLLFNTVLELLTRTIRQEKETKGI/QLGKEEVKLSLFADDMIVYLENPIVSALNLLKLISNFSKISGYKINVQKSHAFLETNNRQTESQIVSELPFTITTKRIKYLGIQLTRDLKDLFKENYKPLLNEIKEDTNKWKNILCS

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3847	34215	A	3887	66	1392	QVLLSFGTPLVLTTKREKNQIDAIKNDKGDITTDPTEIQITSIEYYKHLYANKLENLEEMDKLLDTYTLPRLNQEGVESLNRPITGSEIEAIINSLRPISLMNIHAKILNKILGN*IQQHIKKLIHHDQVGFIPGMQGWFNIRKSINVIEHINRTKDKNHMIILIDAEKAFDKIQQPFMLKTLNKLGIDGTYLKIIRAIYGKPTVNIILNRQKLEAFPLKTGTRQGCPLSPLLFNIVLEVLAKAIRQEKEIKGIQLGKEEVKLSLFADDMIVYLENPIISAQNLLKLTGNFSKVSGYKINVQKSQAFLYTNNRQTESQIMSELPFTIASKRIKYLGIQLTRDVKDLVKENYKPLLKEIKEDTNKWKNIPCSWVGRINILKMAILPKVIYRFNAIPIKLPMTFFTELEKTTLKFIWNQKRACIAKSILSQKNKAGGITLPDFK
3848	34216	B	3888	1	2868	
3849	34217	A	3889	1	1218	
3850	34218	A	3890	1	1893	MKEIETQKTLQKINESRSWFFEKINKVDRPLARLIKKKREKNQIDAIKNDKRDVSTDPAVIQTTIREYYKHLYANKLENLEEMDKFLDTYTLPRLNKEEVESLNRPITGSEIEAIINSLPIKKSPGPDGFTADFYQRYKQELVPFLLKLFQSIEKEGILPGSVYEASIILIPKPGRDTTKKENFRPISLTNIDAKILNKILANRIQQHIKKLIPHDQVGFIPRMQS\WLEVLARAIRQEKEIKG/IQLGKEEVKLSLFADDMIIYLENPIISAQNLLKLISNFSKVSGYKINVQKSQAFLYINNRQKESQIMSELPFTIASKRIKYLGIQLTRHVKEHFKENYKPLVNKIKEDTNKWKNMPCSWVGRINIVKMTILPKIERIGKTKGTETQRGKSCKPTHPVSVISLAESIARDFCLQLNRARSCDQSSYNEVLEADNRAFSLCKGMPFDRLSPISQTPGPSWYQSSPYQPMFLAAPIDIGSRPASMDPIHSRTWHYVTVVILARSRKHQELILSESKQFEEAPPELRSRAPGGFSKPAAGQIKVGLRENLTASMQISPADANLILQDSFLAIFLFQALIVTIYKENEKEEGQERREEALRSTGKNNVWKNTDIDRPESISDSESAGCDY

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3851	34219	A	3891	2	1562	WGEIRAEKLKIPKTGAPLFLQRIAAPRQQRNKTGQRMSLTS*QK*ASEGR**QT/LSKLKEHVLTHCKEVKNLEKRALAKLIKKKREKNQIDAIKNDKRDITTDPTEIQTTIREYYKHLYANKLETLEEMDKFLDTYTLPRLNQEEVESLNRPITGSEIEEIINSLPTKKSPGPDGFTAEFYQRYKEEL/PDKQLQQSLRIQNQCAKITSIPIHQ*QTNREPNHE*TPIPNYYKENEIPRNPTYKGCEGPLQGELQTTAQR\KRGHKQMEEHSMLMDRKKQYCENGHTAQGSTDFGEVQRLRLWQEDDVAEEVSGFFEEDNLKSVAQDPFWESRQVKTIFNCVDTYIAGAKAIAGITQVTCTGNQFAEINQRFLKLKKSWSLYRRFQPWQEECGPSWNPSWTHPSVASSRKDAAAQREAQEGDLQGQEGAEASHAGGPAADHYSGTAHAGRGRALDRGVCVRGHAPPPITELSRPAGCGPHRQGEEAREGDANKKNGFHIQRCSCCLSCKQEHPVLPLVFGLD
3852	34220	A	3892	2428	6109	YPESTMNSNKFTRKKSNNPIKKCQQASQLKALPTQSCSPSSNSYETFLVSPLHPFQFYISFPHYTEMVPPLTPEDYNSRGDFGGDTETNHISKFHRSLEQVQNAASRRSQDGRIGTAPVYSSQRERRRRRVISAFPSEERSSSPAMEQSWMENDFEELREEGFRRSNYSELREDIQTKGKEVENFEQNLEECITRITNTEKCLKELMELKTKARELREECRSLRSRCDQLEERISVMEDEMNEMKREGKFREKR
3853	34221	C	3893	13	391	
3854	34222	A	3894	117	704	WLSAWPRACPDCRVRFPHTSPPCLPCGPEAEPGPGPALRELVQPLPGQLQPPFGMPLPLVPAGSFLICTVWERPRPGLAVGSPPCFPSLH/PTVPVGCPPPSPCL\RPPA*PTTHLHIWPSLLFGPLPALPPPLAASASAGLRKPWLDGLHPSVEPSGLGAAPSPAPPACAWTRPPHLHPSSFSSCVPQISSLFLCF

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3855	34223	A	3895	1	1185	SAASSVLYVHNEPQVHGAHQKIHPIHPSLHYCLAHIISQDLHTSMNALGLFGVG*EQGLQEKSNLSSTHHEPGHGGQDAAGARDGARGRGGS\TGSAAGERGGRTVPHWA/GQPAEAGGAG*PRGPQLRRSPPP/RLPPRAGSSANTRNSVLL*FF*AVCLWADHYPL*TLISSS*MAGRWRSVPGIPTSPTK/PPPPPPPPPPPPPPPPGSFLSEP\VWSTA*NSTCPPRRCRSASGGPIWCPCRP/PAPPPAPPAPPPLEATEESLEEG\GGRASRSANMFAPTAPAGSSWHRARWG*PAWKAGAAGTRGAKCGQFVPSASSAP*LAGGWPGAGGQRGARRAQKAWCCRPGTSL/APGPELFPESALVQAGSAPPPPPPPPPPLCLLLLRAESEGAVLM
3856	34224	A	3896	192	477	
3857	34225	A	3897	2	1782	RAAARKEHQGSAT/RAERA/PRTPKAS\GRG\SPVPTSGTVTARTGTAPRGLSAEDGRRRGRP\IGIPFTDHSSDILSGLNEQRTQGLLCDVVILVEGREFP\THRSVLAACSQYFKKLFTSGAVVDQQNVYEIDFVSAEALTALMDFAYTATLTVSTANVGDILSAARLLEIPAVSHVCADLLDRQILAADAGADAGQLDLVDQIDQRNLLRAKEYLEF/YYQSNPMNSLPPAAAAAAASFPWSAFGASDDDLDATKEAVAAA\VAAVAAGDCNGLDFYGPGPPAE\RPPTGDG\DEGDSNPGLWPERDEDAPTGGLFPPPVAPPAATQNGHYGRGGEEEAASLSEAAPEPGDSPGFLSGAAEGEDGDGPDVDGLAASTLLQQ/MDVIGGPGGG\RGGGQRRGVAGRRQGRHGLLPEVLQRRPRRRRLPGLVAEGGEEDPSQGLPEVPHLREGHPGRRQAAATHPHPHGREALRVQHLQGPLHQDTSTSTLQKPGSPRPL*VTAGR*AGQAEGAHAEAHGREAVPVPAVRRRLCPQLRPEEPHARAHGPAPLPVRQLLQDLRPLRPPAQTPQERRLQRRPLAPAVPASPCVLWAGGCPDPQPW
3858	34226	C	3898	162	356	

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3859	34227	A	3899	3	2289	GELHGVAEQAEGDPREGSPGPAEQASGTELREVPGPHWPLHPPEAPVCQHYHRPMVQKGN*GSVWGRGESLVQG/AHGQTSQRSVQMTGGGAWTGQTSQRSVQMTGGGGTPRGSRSSSPRTT\TPGTAEDTEGEPAGAGEQAAGRPVRPLHGHPGAGQEAAAGVRELPPAEPAAHLHPQPALLIQQHPISHARSQHPRRPCCLPGPGLRAGGTAEGLPCAFCSQRDERAEGRERDLEGGGEAASGPGRQAQAPGQGGHLGPPLTPAAPLPWWLEGHHREATGRPRGG*GRPPGRGPTGRRKASRAQDISSGQNLPRGHPA*VASPRHEPPAHLQPAARDHCRGA\PGSQACPADRGPANGTPPPLPARSSPPSP\GMSVASPWTASCGPPGPPP*P\IGPEALPEGGPALPPKPPPVPAPSEPPQQPPGPCCSPQRPPAPGPEGQRSRGLGGAHRTAGAAQCPGGHAGPSPGGGTAPAPGPAAAAG*GQGRQCQAKGPAHTRGDAALPTSRLRL*GP*E*GDQGSSG\AAGLSGGRHTQPAGPGRAQRTEAAATQDCALDKPLDLSEWGRARGQDTPKPAGQHGSLSPAAAHTASPEPPTQSGPLTRSPQALSNGTKGTRVPEQEEASTPMPPDLDGHP\GPARLKC*DQSPTNWMRQTPQAA\SGPELPGGG\PTSTTGEGPECICTQEHGQGPPRK
3860	34228	A	3900	3	3169	ASQLVLTLAYQANCVSVSYTDLLGKPGGSYFTFLYVLNIRSRSRLKKDYDDFRRQPDHDTFNRELWTTDEGEGDLGKDSPKGEISKSIDSTEPLDILEKDHFDSDDMKLSEIDFPMARSKLLKKELPSKDLPKTLLKTLKRQSKQTDYVDDSTKELSPRKKAKLSTNETTVENLESDVQIDCFSESKHTEPSFPESFASLDSVPVSTLQKGTKPIQALLAKNIGNKVTLTNQLPPSTGRNALAVEKPVLSPPEAS

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3861	34229	A	3901	33	1227	HHLRGTGQRAGQQLPPGMKMGRAGPPGPWCEHTT/PPSRGRPTSSGGPTLAPALAELSPRPQTPSPSISSLPMITSLPGGTGPLCLRPLSWEKPGSATGK\RGSQQEVDVGPSPGHTAPSKSHGQGPVGSPSARQGCGPASSALQRRREPGGGPRGHPAGPHGGCVLPPWPGCPGNTMQRL*GFHTRAMNTQSGAGPRTAPSPRAQGAQGRPSKSCSGASQGPCPAVGPH*APGEDRVRHPLASISGTTRAHGRPSQQREPRNKSTRADSRSPRTVPPHGPPGPSLPRGR\PAQPGPGV*RNGISVGAGRFPPPFTAPCGQQARPGAG\NRGAGSGA\PEL*GGLGRDPGSSGCEVPGGRAGG/PPRT*HFLARPAPPSPPQGLPRPPKVLGLQA*ASAPS
3862	34230	A	3902	124	1183	DNRAVFSPTGRR\DRGGGGPAGTLARV*SAPGAFGV*STRTHVAGVQMPPVPGTCDVCTRPCSPVSRPPRASTAVAAAAS/SGPRQPRHPRHTSPMPPPAALRPPAGPRGLAPGG/HTAPPATAAPVELQHPLLRLQTGPPLGPPTGPA*EPRAHPCIRGLLPAGSGPPPRRQGHPEPPRLHTAACSPCQPQRALESSCPPRAFPGTAAHWLLGTGDWLL*PAAQAALASQEWALPGICLCNSLSEPTGRVILASQLAPCIRLGCRKRSLAKAPKLISGGAGAHTPTPEPTCFSVSVLGTSPPAAGGPRGQESVVSSPVTMGT/VPAWAIPSLGCRGEASLDHPAGQLPARGQRSRRH

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3863	34231	A	3903	174	1599	VLHAVGNQVQGCPGPEVHVCG WRPGCVRLLQLHVVGRADGPE CDLCAVWPGGGDV*PAVPGAV PHVTQCEPQGHPYGEGTGAGA YCAALCGPPGARGHCGQEARQ PQVRTCQGQERRRDCQDLL*E AGGQEAPGAERPSAG*ASRGTP RAAATHPPRTASPGEGQHV*VP AHVGGARPGAWQRHPGLHQY HRPQHLEPPAQPDEPHQDP*HL PGQRPAPAVEAEPGQQAPS\KP CPPPEPSAPQDGVPAENGLPQG DP/GAIAPRAQAPDSPCGRCTSP GQQ*YWLGPGAPQRGSSPEWD RP*ATQDGRPRPRPTPAAAICDP G*PREPRGGAPQWAGWGGRRR **RLRNPQ*PGQP\SGSSGRGPG PRRPSVASSVSE/RVLRGERALS PSPEAPLRASGQRANPTTAPAA ECPPYNPRDLCWTPGWLPMGP ESGKRRSRCVEEDAGPALHRQ GGTDGET**TGRGGNRPGPYGR
3864	34232	A	3904	331	1120	HKDRFWQLQNDSCFLHSPGER QWLGGPRSDTFGPQVLFGHVGI CSQRA/HPAGPGHRGLPEGR*PP HRSQRHPPRSRKPYLA*PPDMC VATDRRTQTPRDFPPLGR*KPH GTLRSAACPAGRVSPSPRPRGL PAPPPKSHLCG\PGVRGR*QLLP PHPGSPKGERGWTASPGAARG GPGPAPAPRP\RASWSQPSVTFP LPLAGLA/GHPGSRTEPAWKAG GAAARPGPELPRDLLQAGSTDT ASGEQLAAGPWTGKEISGRARP RL
3865	34233	A	3905	2	415	YTILTEK*KLSKLST*W\VHQDQ LQKREELSMEILNK*DQDSEAY PQRTVTGEETWLYQYDPPPLPR SLPPPQTHTAPVGA*S/DWGG*E LPPGLNGDKLAHHSPTPFLSFSG LLFVDWL*SQLLSLFGLFTQGVI RIFI

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3866	34234	A	3906	1	4527	MGFCCRECRPRLLKGRPCIQHAGPVAAFKVATPYSLYVCPEGQNVTLTCRLLGPVDKGHDVTFYKTWYRSSRGEVQTCSERRPIRNLTFQDLHLHHGGHQAANTSHDLAQRHGLESASDHHGNFSITMRNLTLLDSGLYCCLVVEIRHHHSEHRVHGAMELQVQTGKDAPSNCVVYPSSSQDSESNHGNNFRIHVSNGLLMRGPRPLDRERNSSHVLIVEAYNHDLGPMRSSVRMRKLRQSTALAQHWTGTALDR
3867	34235	A	3907	1	2180	MALTFPCRKFEWYGRRQPEVRYSVPASHQLKATDADEGEFGRVWYRILHGNHGNNFRIHVSNGLLMRGPRPLDRERNSSHVLIVEAYNHDLGPMRSSVRMRKLRQSTAL\DSTGQAQHWTESRSGSPGSPVAPTCSART*QTSAS\VHLCLSGKSHHAWPP*TPFKLYYVH\EYSAHIHKENLVLVIVYVEDINDEAPVFTQQQYSRLGLRETAGIGTSVIVVQATDRDSGDGGLVNYRILSGAEGKFEIDESTGLIITVNYLDYETKTSYMMNVSATDQAPPFNQGFCSVYITLLNELDEAVQFSNASYEAAILENLALGTEIVRVQAYSIDNLNQITYRFDAYTSTQAKALFKIDAITRILGTQMDTKMNKTLLSPQRVLRLEVEMELIQDANQSATRRCAENYNRGVVEPLRAQQSYLAGEAGRLHGRGGFPVECEREEGIQQTECPGEVMPDRGSDMEGVITVQGLVDREKGDFYTLTVVADDGGPKVDSTVVSGTRVYITVLDENDNSPRFDFTSDSAVSIPEDCPVGQRVATVKAWDPDAGSNGQVVFSLASGNIAGAFEIVTTNDSIGEVFVARPLDREELDHYILQVVASDRGTPPRKKDHILQVTILDINDNPPVIESPFGYNVSVNENVGGGTAVVQVRATDRDIGINSVLSYYITEGNKDMTFRMDRISGEIATRPAPPDRERQSFYH

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3868	34236	A	3908	603	1395	RGRPRGSPIFPTRAPREKKR*EEVGGHKREQTG*GGGERRKPPNPQHEPKERGWCSRVPEEPQ/RKRRSARARPKKL*REKRRRGRPKRCLW*TGRHPSHHPRTHQC*F*WRK/REEGKERKKEQPAHAGQKRRKAARHRRRRRRRERTDEKNRTWTRRRREKAGQDEKREGEHGQKRSQQGRESRRDGRARTRKERRQKRENDNRARRRQQAEREKTKSVKRRQTTQQAEEVRQARENEAREPQQRRQHSRRRKEKEEMRAPRSKQ
3869	34237	A	3909	1	548	
3870	34238	A	3910	1	1803	
3871	34239	A	3911	1	279	
3872	34240	A	3912	1	506	MCYSRQSNLGTFGEGKIKGSEVIDECPRSSRYQDLQELQNKTKLTVLEGDILDESCLKRACQDMSVIIHTTSIIDIIGVTHRESIMNINVKRTQLLLEACVQATVPVFIYTSTPEVAGPNSYKEIIQNSHEEEPLENT\WCSPS/PYKKA/LARSGI*ATLQLGGSQEECT
3873	34241	A	3913	3	621	AGQQTVEIDLRHRIQLP\DLENQRNFNELSRIVLEVRERVRQEQQEGGHEAGEGRGRQGPRESQPSPAQPRAEAPSKGPDGTPGEDGGEPGDAVAAAEQPAQCGQGQPFVLPVGVSSRNEDYPRTCRMWNSTFQTYKKEVCLPRHSMHPGPWAICCECQTRFGGRLPVSRVEAALPYWVPLSLRPRKQHPCWMHAAGTTAGGSAVMS
3874	34242	A	3914	1	430	RHRIQLPDLENQRNFNELSRIVLEVRERVRQEQQEGGHEAGEGRGRQGPRESQPSPAQPRAEAPSKGPDGTPGEDGGEPGN\AVAAAEQPAQCGQGQPFVLPVGVSSRNEDYPRTCRMW*GCGGYWGLKVGQHGLQRGPQPHT
3875	34243	A	3915	2	1175	
3876	34244	A	3916	1	256	HLRIHTQESSYVCDECGKALTSKRNLHQHQRIHTGEKPYECSKY\G*PFGLLPQLGHLEHVYSGEKPVLDICRFGLPEFFTPFYW

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3877	34245	A	3917	1	1396	MRPQLAGRDHHRGAATLLLER PGRLVTHFRQRRGAVRYGGGK STTQHLSQRRLSGPNDHTKGLV WLLEHILQRLVSFVKLQATRTF TRTYITYAWFLPWGFSGVLCGT PVDTCWALKHQRIHTGEKPFEC SECGKAFNGNSSLIRHQRIHTGE RPYQCEECGRAFNDNANLIRHQ RIHSGDRPYYCTECGNSFTSSSE FVIHQRIHTGEKPYECNECGKA FVGNSPLLRHQKIHTGEKPYEC NECGKSFGRTSHLSQHQRIHTG EKPYSCKVCGQAFNFHTKLTR HQRIHSEEKPF*L/CVDCGKAFS AQEQLKRHLRIHTQESSYVCDE CGKALTSKRNLHQHQRIHTGE KPYECSKYEKAFGTSSQLGHLE HVYSGEKPVLDICRFGLPEFFTP FYWKEEKKCGRKMRNEVVHK VSFFLVVPIALSSLLKKKWKML KKEKAQDPTEYGNLEDDNSQQ
3878	34246	A	3918	1	547	MDSQRPRER/QRERERQSERQR HTQRMHREAETEDERDWKGH DTKTRRQRQRKRAEEGQCREH DRERRRD\RTGERREKQRKSTQ QSRKPSEEPHREKTQIKRERGPE QGELERGQCTERNRKA/GTPEC *TDPHIWTPHPARSAPAHPPDH TAAKYRPPYRSHHSGITHQHPR AASTLKLWPKP
3879	34247	A	3919	1	399	
3880	34248	A	3920	3	872	KSKLKSEQDGISKTHKLLRRTC SSTVKTDDVCVTKSHRTFGRSL SSDPRAEQAMTAIKSHKLLNRP CPAAVKSEECLTLKSHRLLTRS WSGDPRCEHNTNLKPHKLLSRS YSSNLRMEELYGLKNHKLLSKS YSSAPKSSKT*/VFSKEP*RRRG RKALSLPQGLFGYP*HHLHPSSS QLAPNGAKCIPVRDRGFLVQTI EFAEQRIPVLNEYCEVCDEPHV FQNGPMLRRGRDVCEWAKKY ANSVVRKKFCRLSIARRSRYRA DMDLLRMSNFILTIIYKQKLNL
3881	34249	A	3921	3	218	CCRSHQGAGEGGHLSVQLLWQ YRWMWCSWGPV\FQFHTDLEL VAWRCVGLDPGCQQLDIGMQT LIGDHICVF
3882	34250	A	3922	1	1055	

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3883	34251	A	3923	3	962	RSMRQKVNKDIQDLISALPQAD LIDIYRTLHPKSTEYTFFSAPHR TYFKIDHIVGSKALLSKCKRTEI TTNCLSDHSAIKLELRIKKLTQN RTTTWKLNNLLLNDYWVHNE MKAEIKMLFETNENK/DETYQN LWDTFKA/PSIILNGQKLEAFPL KTGTREGYLLLPLLFNIVLEVL AMAIRQEKE/IKGFQLGKEEVK LSLFADDMIVYLEDPIISAANLL RLISNFSKVSGYKINVQKSQTFL YTNNRQTESQIMSELPFTIATKR IKYLGIQLTRDVKDLLKENYKP LFNEIKEDTNKWKNIPCSWIGRI KIVKMAILPK
3884	34252	A	3924	1	1452	MGDFNTPLSTLDRSMRQKVNK DTQELNSALHQADLIDIYRTLH PKSKEYTFFSALHHTYSKIDRT VGSKALLSKCKRTEIITNSLSDH RAIKLELRIKKLTQNRSTTWKL NNLLLNDYWVHNEMKAEIKM FFETNENKDTTYQNLWDTFKA VCRGKFIALNAHNRKQERSKID TLTSQLKELEKQEQTQSKASRR QEITKIRAELMEIETQKTLQKSN ESRSWFFERINKIDRPLARLIKK KREKNQIDVIKNDKGDITTDPT EIQTTIREYYKHLYANKLENLE EMDKFLDTYTLPRLNQEEVESL NRPITGSEIVAIINSLPTKKSPGP DGFTVEFY/QEGN*AGEGNKGY SIRKRRSQIVPVWR*HDCISRKP HRLRPKSP*AGKQLQQSLRIQN QCTKITSIFIHQ*QANRKSNHE* TPIHNCFKENKIPRNPPYKGCEG PLQGELQTTAQ*NKRGYKQME EHSMLMGRKNQYRENGHTAQ

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3885	34253	A	3925	1	1251	MKAEINMFFETNENKYTVYQNLWDTFKAVCRGKFIALNAHKRKQERSAMNTLTSQLKELEKQEKTNSKANRKQETTKIRAELKEIETQKTHQKINESRSLFFEKTNKIDRPLARLVKKKREKNQIDAIKNDTGDITTDPTEIQTTIREYYKCLYANKLEYLEEMDKFLDTYTLQRLNQEKVESLHRPITGSEIEAIINSLPT/KKSPGPDRFTAQFYQRY\DGMYLKIIRAIYDKPTANIMLNGQKLEAFPLKTGTRQGCPLSRLLFNIVLEVLARAVRQEKEINGIHLGKQEVKLSLFADGMIVYLENPIVSAQNLLKLISKFSKVSGYKINVQKSQAFLYTNNRQTESQIMSELPFTITTKRIKYLGIQLARDVKDLFKENYKPLLNKIKEDPNKWKNIPCSWIGRINIMKMAILPK
3886	34254	A	3926	1	1203	
3887	34255	A	3927	1	1233	
3888	34256	A	3928	1	951	MKREKNQIDAIKNDKGDITTDPTEIQTTIREYYKPLYTNKLENLEEMDKFPDTYTLPRLNQEEVESLNRPITGFEIEA/INSLPTK*SPGAEGFTAEFYQSVGSSGQGNQARERNKGYSTRKRGTQIVPVCRWHDCIFRKLHGLSPKSP*ADKQLQQSLRIQNQCAKITSIPIHQ*QTYREPNHE*TPIHNCYKENKIPRNTTYKGCERPFQGELQTTAQ*NKRRHKQMEEHSMLMDRKNQYRENGHTAQGHL*IQCHPHQATNYFLHRIGKNYFKLHMEPNKSLHSQDNPKQKEQSWRHHAT*LQTILQGYSHQNSI
3889	34257	A	3929	1	814	

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3890	34258	A	3930	1	1545	HQLKVQFRIIISIRSSCDGSAWGVAPTFKTRGARSRSRAAIRLGAADLDEVKSSLVNESENQSSSSDSEAERRPQPVRDTFQKPRDYFAEVRRPQDSAFFKGPPYPGYPFLMIPDLSSPYLSNGPLSPGGARTNSSPAPKETWICARFGGVSLSFLEIGSRVLLLGRDVNRSSSLLPAQIPIACHFAVDGGNFIRGKGAYLLTFDLFGNWGLFFLIEIAVWELSAHSSGQSEDALELSRGTCSSSLQLCWTAKALVGKGLDGGPVCKNSGICSTRTKTQEQMSFMEALYQEGFLRETVVQAVRKVPQTPRKAVLEVLARAISQEKEIKGIQLGKEEVKLSLFADDMTVYLENPIVSAQNLLKLISNFSKVSGYKINVQKSQAFPYTNNRQTESQIMSELPFTITTKRIKYLGIQFTKDVKGLFKENYKPLLNEIKEDTNKWKNIPCSWIGRINIVKMAILPKVIYRFNAIPIKLPLTFFTELEKTTLNFIWNQKSR\IGKKILSKKNKAGGI
3891	34259	A	3931	693	1464	ARAEVKLSLFADDMIVYLENPII*ARAEVKLSLFADDMIVYLENPIISAQNLLKLISKFSKVSRYKINVQKSQAFLYTNNRQTESQIMSELPFTIATKRIKYLGIQLTRDVKDLFKENYKPLLNEIKEDTNKWKNIPCSWIGRINIVKMAILPKVIYRFSAIPIKLPMTFFTELEKKNWLAICRKLKLDFFFIPYTKINSRWIKDLNVRPKTMKTLEESLGNTIQDIGIGKDFMTKTPKAMATK/DQKSFCTAKETTIRVNRQPTEWEKIFAIYPSDKGLIS

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3892	34260	A	3932	211	2519	ENRKSNCLCLQMA*LYI*KIPSSQPKISLS**ANLAKSQDTKSMCKNHKHSYTLITDKQRAKS*VNSHSQLLQRE*NT*ESNLQGM*RTSSRRTTNHCSTK*KRTQTNGRTFHAHG*EESIS*KWPYCPSKC/KRTEIITNSPSDHSTNKLELRIKKLTQNHTITWKLNNLLLNDSWVNNEIKAEIKKFFETNENKKTTYQNLWDTAKAVLRGKFIALNAHIGNLERSKIYTLISQLKEPERQEQTNPKASRRQEITKIRAELKEIETQKTLQKINESRSWFFENIKIDRQLARLIKKKREKNQIDTITNNKGDITTDPIEIQTTIREYYKYLYANKLENLEEMDKFLDTYTLPRLNQEEVESLNTPITGSEIKAIINSLPTKRSPGPDRSTAE/FYHRYKLELVLFLLKLFQSTEKEG\GRDTTKKENFRPISLMNIDAKILNKILANRIQQHIKKLIYHDQVGFIPGMQGWFNICKSINVIFQYTNNRQTESQIMSELPFTIASKRIKYLGIQLTRDVKDLFKENYKPVLNEIRGHKQMEEHSMLMDRKNQYCENGHTAQGNL*IQCHPHQATNDFLHRIGKEEVKLSLFADDMIVYLENPIISAQNLLKLISNFSKVSAYKINVQKSQAFRYTNNRQTESQIMSELPFTIASKRIKYLGIQLTRDVKDLFKENYRPLLNEIKEDTNKWKNIPCSWVGRINIVIMAILSKVIYRF
3893	34261	A	3933	2	1304	
3894	34262	B	3934	141	2008	

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3895	34263	A	3935	1	1845	MVISVDAEKTFNKIQQPFTLKTLNKLGIDGSYLKIIRAIYDQPTANIILNGQKLEAFPLKTGRRQGCPLSPLLFNIVLEVLARAIRQEEEIKGIQLGKEEVKLSLFADEMIVYLENPIVSVQNLLKPIRNFSKVLGYKINVQKSQAFLYTINRHTESQIMSELPFTIATKRMKYLGIQVTRYVKDLFKENYKPLLNEVKEDTNKWKNIPCPWIGRIN\ILKMAILP/KELEKTTLKFIWNQKRACIAKSILSKKNKAGGITLPDFKLYYKATVTKTAWYWYQNRDIDQWNRTEPSDIIPHIYNHLIFDKPDKNKKWGMGSLFNKWCWENWLAICRKLKLDPFLTPYTKINSRWIKDLNVRPKTIKTLEENLGNTIQDIDMGKDFMSKTPKAMATKAKIDKWDLTKLRSFCTAKETTIRVNRQPKEWEKIFAIYSSDKGLISRIYKELNFTRK\NNPIKKWAKDMNRYF*KEDIYAANRHMKKCSSSLAIREMQIKTTMR/YHLTPVRMAIIKKSGNNRTRENYFKIHMESKKSQNSQGNRKEKEQSWRHHATRLQTIVQGYTVAKTACYWYKNRPTDQSNRTENQEIRLHTYNHLIFDKPDKSNGETTPYSINGARITG
3896	34264	A	3936	1	700	
3897	34265	A	3937	1	3489	MKSGHPEKEQDNSDVQETREITIRGLLCTALMRHSTGAIAYLGVLSGSASLKLAGVPLRCCEGDKDAGHPLETQTALCERGRGARSLVGNTIMTSQPVPNETIIVLPSNVINFSQAEKPEPTNQGQDSLKKHLHAEIKVIGVNLIQNVLERGWGKCQEMIYVLGLDICRPFFVSRVSEEGRMGQRGEEDANSLDFPPASLLCLICQEQGVNGESCSPVGMYHREIVPVYEVLSVITGLQIQVFSGKEADSVIKRS

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3898	34266	A	3938	120	1331	TSLGPIYCAVRHTSSCRKVGSSRCQHGCQLSVRLQLDQAHHKQLPWLAPKNAVVPKSLEDPQGRKEGVTALTPEAPRSGPPKRLQLFPPSLCPNCSKQGAYFSPFGVTATLLATPFSRSRVLVLQPGRMRYADKWRVSKMKRCCIEQWNSSEKTHSARASHSLQRQRGGPRVGGSSLQAGCHVISAALSKEEALEWVASFCRQIVQSYLRPLLCSGADPGAFMDLRGEELRSLELSLSYTPPSNEFKISMKLEAQDPRNTTSTCIATVVGLTGARLRLRLDGSDNKNDFWRLVDSAEIQPIGNCEKNGGMLQPPLGDSFHCDVRVSILDLFCFLLSELPFTIDTKRIKYLGIQLTKDVKDLFKENYKPLLNE/IK/EDTNKWKNIPRSRIG*INIVKMAILPKDFG
3899	34267	A	3939	1	1421	MDSMSGGGQYRKINGNPTSVKCPLLLLPAILTPEPVNRWRQSCKAFARHSPLAFRVTISTSTFFDGLLVTGLYTSTSVQASQSIGGSSAFGFVLEVLARAIRQEKEIKGIQLGKEEIKLSLFAGDMIVYLENPIVSAQNLLKLISNFSKVSGYKINVQKSQAFLYTNNRQTESQIMSELPFTIASKRIKYLGIQLTRDVKDLFK\ENYKPLLKEIKEDTNKWKNIPCSWVGRINIVKMAILPKNWKKLKFIWNQKRAHIAKSILSQKNKAGGITLPDFKLYYEATVTKTAWYWYRNRDIDQWNTTEPSEIMPHIYNYLIFDKPEKNKKWGKDSLFNKWCWESWLAICRKLKLDPFLTPYTKINSRWIKDLNVRPKTIKTLEENLGITIQDIGMGKDFMSKTPKAMATKAKIDKWDLIKLKSFCTAKETTIRVNRQTTKWEKIFATYSSDKGLISRICNELKQIYKKKTNNPIKK

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3900	34268	A	3940	3	1566	IQTTIGEYYKHLYTNKLENLEE MDKFLDTYTLPRLNQEEGESLK RPMAGSEIEAIINSLPTKNSPGP DRFTAEFYQRYKEELLISNFSK VS/VIQNQWEKITSIPIHQ*QTNR EPNHE*TPIHNCFKENKI\LGIQL TRDVKDLFKENYKPLLSEIKED TNKWKNIPCSWIGRTNIVKMAI LPKDKTSKYIDVDENEGSHCGK RKYKYGMEKALEILARAIRQEK EIKGIQLGKEEVKLSLFADDMI VHLENPIISAQNLLKLISNFSKV SGHKINVQKSQTFLYTNNRQTE SQIMSGLPFKIATKRIKYLGIQL TRDVRDLFKENYKPLLNETKED TNKWKKNILSSWIGRINIVKMA ILPKVIYRFNAILINLPMTFFTEL EKTTLKFIWNQKRACIAKTILSQ RNKAGGITLRDFKPYYKATETK TASEMKYYLENKIPFKVLHMV YNVPTHPPFIGDLHPNTKVVSL PPNITSLIEPMNQGVISAFKDCY LRKTFVQAVATPEGETEMTVM QFWKDYNT

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3901	34269	A	3941	1	2580	MVKGSIQQEELTILNRYAPNTG APRSIKQVLSDLQRDLDSHTIIM GDFNTPLSTLDRSTRQKVSKDI QELNSVLHQADLIDIYRTLHPK STECTFFSAPHRTYSKIDHIVGS KALLSKYKRTEIITNCCSDHSAT KLELRINKLTQNRSTTWKLNNL LLNDYWVHNEMKAQIKMFFET NENKDTAYQNLWDTFKAMCR GKFIALNAHKRKQERSKIDTLT SRLKELEKQEQTLHSKDSRRQE INAEKAFDKIQQPFMLKTLNTL DIDETYLKIIRAIYDKPTVNIILN GQKLEVFPLKTGTRQGCRLSPL LFNIMLEVLARAIRQEKEIKGIQ LGKEEVKLSLFADDMIVYLENP IISAQNLLKLISNFSKVSGYKIN VQESQAFLYTNNRQTESQIMSE LP\FTIASKRIKYLGIQLTRDVKD LFKENYKPLLKEIKEDTNKWK NIP\CSWVGRINIVKMAILPKVI YRFNAISNKLPMTFFTELEKTTL K\FI*KQKRACIAKSILSQKNKA GGITLPDFKLY\YYKAIVTKTA WYWYQNRDIDQWNRTEPSEIIP HIYNHLIFDKPDKNKKWGNDS LFNKRCWENWLAICRKLKLDP FLTPYTKINS\RWIKDLHVRPKT IKTLEENLGNTIQDIGMGKDFM TKTPKAMATKS\KIDKWDLIKL KSFCTAKETT\IRVNRQPTEWK KIFTIYPSDKGLISRIYKEPKQIY

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
3902	34270	A	3943	5	2130	QRLRRQHRLEQKTRSTTCHMR QSTTRSAERADTRIESMPT*TTP *HTDDVP/SHCTNSTHTATTSPS THNHQQTLTRVANVAQIRRTDI SSIAATEWISTINTHNYACRTRA VSQRRYVSDFEKRERPTSNTPE PRFRLVVSTPTLVGTTQGTYQP PPARSRISIASHLLPPLSLLPSSL DLDGRSTLACSSSVSQFSGSRGS PSSYIVATTRVISDVDYDMTTY YNSTITPIS/PSARS*CQRSVHLL LSSHRTYRHPLVSRHTSQEHSL GGPLHRH*YNPVGSRAAAWAS KSALV/SVSLEALVVSALI*LVA TRQRLVGICRTTPIRARSSVVR* VTRYQPNQRAPLIHATYHLLDR GQHPQSMQTISHWTTPPCWCL VCGKKSSLPCCSTSSMSTRRNQ YDTLSLTTSWVL*SSIFWLAFIL LPRTSLPWPTVS*LAANA\SSGS TPVNSSFRT\SVRRSKLVVPANE IETPSFVVVTKFSRSASSYDCSIE YASTYAINITIVNSYVFA/PTHTT REHTISYALTSPGQPQNKTRIPE LQWAF*AVRPSTQ/PSTVIYHAP TSQAIASCALHSLLGCLLGSAT APLPPTWTTPPPPPQLRTT*STG SLPHPPSC*TRP*PLAPRN*PFTG MSSQHCIPT*PQLASHSIALRG/S RARPTTSQTSIAS/SHSHS*LSHV Q*RPLSDQRSPLDHHAHSSILYA RASRISCLRVCAV
3903	34271	A	3944	254	884	MTPNYTSRLFLHMGVLFYPFYR RLT*HIRTHINLKGWK/NRHFM QMDTKNAEKALDKIQHRFMIK TLSKISIQGTHF\KIIKAIYGKSTT NTILNGEKLKAFPLRTGIKQGCP LLPLPFNIVLELLARAIRQEKEIK GIQIGKEEVKLTLFADDMIIYLE NSKDSSRKLPELIKEFSKVSRYK VNLHKSIALLYTNSDQAENQIK NSTSFTI
3904	34272	B	3945	52	843	

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3905	34273	A	3946	1	831	MEMLYCLIAEAGHISSRMATNTANSAGLKPTCVCVALPLPPGRSAPHRSCSQAGRELPGQGPRYYRHLPQLSILHSIGEGQGCGFWSERSFKGYPERPAGAAGVCRLQGCGRRGRGAPFRTTDFSSRPRGAAERADQGPRAGSPWPRTTSGAQRGRAQGQGHTARRRGNSNPGPSRARQASRRRRPATSGPPRGSPRPDRPRRRSPFYRSSSRETSRPPEGPRRPRAPALSAPAPGQPARPRPREPVPCGAVFTARDRLRPPAATSHAPFSAANPRR*HRPGGPGARRLGDAQLSRRST/SGAPRCSQTRSR*PTCVCVALPLPPGRSAPHRSCSQAGRELPGQGPRYYRHLPQLSILHSIGEGQGCGFWSERSFKGYPERPAGAAGVCRLQGCGRRGRGAPFRTTDFSSRPRGAAERADQGPRAGSPWPRTTSGAQRGRAQGQGHTARRRGNSNPGPSRARQASRRRRPATSGPPRGSPRPDRPRRRSPFYRSSSRETSRPPEGPRRPRAPALSAPAPGQPARPRPREPVPCGAVFTARDRLRPPAATSHAPFSAANPRR
3906	34274	B	3947	250	281	
3907	34275	A	3948	3	639	DHTCRLRQRLRLRVLVGPVPGAGPAG*KGCYGGRSANHHGAPASCHLARSSCGPRLPGRYSAQQPRARCAASGLCGWTAPAADPVPSEVLASQEVQLLCAGE*SGSCGPTHADLQPSPGGTGEDGAARAKRDLPGSVGERAAAPASGRLRACPGRPAGAPGPRARPPGGTAALAQPPRPQGAAARPPSGIGWP\GNNGSAQSKGRALMEQAAG

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3908	34276	A	3949	161	2377	SLFHGKVCHFLHEPLPLVYLSL CTGYQLFKPSLISWLEEEEELST LPRVLQEWKMCLKTKGPALW QDNFCLKTLNGIQLARNQNGEE LYDCKQCEDVFCKHPCLKTNM STQNRGNTSECIQYAKDLLSLY NKTSTIRKVSVFSKHGKSFRL\F *MFRSRESVHKINPLK/CTDYGK AFIYQSYLEAHRKTQSGEKLNE WKQCGEAFTHSTSHAVNVETH IIKNPYECKECGKDFRYPTHLN NHMQTHIGIKPYKCKHCGKTFT VPSGFLEHVRTHTGEKPYGCKE CGKAFGTSAGLIEHIRCHAREK TFKCDHCGKAFISYPSLFGHLR VHNGEKPYEHKEYGKAFGTSS GVIEDRRSNTGQKRFDCDQCG KVFVSFSSLFAHLRTHTGEKPF KCYKCGKPFTSSACLRIHMRTH TEERLYQCKKCGKAFTKCSYLT KHLRTHAGEKPYECMKCGKAF TERSYLTKHLRRHSGEKPYECK KCGKAFTERSDLTKHLRRHTG DKPYEYKDCGKAFVVSSSLVD HLRTHTGYKPYKCNACEKAYS RSCVLTQHLKTHAAEKTSECN ACGNSFRNSMCFHDRLKTLTKI KPYKCKDCGKAFTCHSDLTNH VRIHTGEKPYKCKECGKAFRTS SGRIQHLRTHMGEKPFECDQCG KAFA\FSQLVLHI*KHTREKPCG CEECGKTFAVSSSLTEHVKIHR
3909	34277	A	3950	6	455	GLLHERQAEARCSICLDYLRHP MTTDCRHYI*SARIHQCW*ELQ DISPCPVCLQHCPDKNLKRNFQ LCHMTDIAKQLLTTARRKRKL QGEEPVCRKSDVALFCEKDPEL LCHQYRVSLDH*DH/SPMPIEQ AAAKHRKQFESYIEPLEKQV

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3910	34278	A	3951	2	1009	WNGHRMN*MQSSNGLEWN/QSSNGKEWNHRIESNGIIIAWN\QWYQHQTEKNGIFEWNRRESSNGPEWNHVMEWNG/DNPWTRMQSSSNGIEWNHRMDSNGIIFQWNGNGNHRIGIEWNYDQ\SNEWI\QWNQHQTEKNGIIKWNRRESSNGPEWNHLMEWN/ENNPWTRMQSSSNGIEWNRMESSNGLEWNNH*TESNGSVESSSDGNER/QSSSNGIAWNHHKMESNGINIKWNQMESWN/WN*MNRMELSSNGIEWNQHQTEKNGIIEWNRRESSNGPEWNHLMEWN/ENNPWTRMQSSS/NWNRMESSNGLEWNN/QLNGIEWNHHRMEMNGIIIEWNRIELWN
3911	34279	A	3952	1	1494	MASLLGAPRLAGWASGAGALSRGWAIRPADTGGNLGPVPRVPLPPDPVLTARWAPGVNSGSQFSCHCQAPILEMGHKGSSPGLGDAEVRAITVQCIRPIDGPQQPPGGGSAGRRLTIPASTQEWAQLPVGRVLANVLTEGGDTGNQPIPQRSLCRPQPCSHAETWGEVEAQVPAQSNREQPAAAPGCGPGRGETGARPETTFSPRRAPPNPYDEEGVRWSLEFMLCGTDGPVQPVQHQEGPAARLQLIRGGSLILESEGTLRG/SPVLQTDQPASHLLHTQGFWA/AALSAVCL/HQNIIHSGSALLAPATRAAWEQIQRSEGGTAQLLRRLEGYFSNVARNVQWTYLQPFVIVTTNMILAVDIFDKFNFTGARVPWFDAIHEAFPRELESSISFPANFFKPPEEKEGPLVRPASRKTTPQTTRPGPGTEREAPISR*KRHPDDTG*FTFTLGIVYCTPGQLPPEPYDPNRRSLWLPHWPIINTSMVSALVYSEGAPLPSPL
3912	34280	A	3953	1	681	MGQLLDKNTPSHGARTREECGRERLCVSPSQTGDTPRTSAYLCVGGPAWSPLSESRPAGSSGCPWIKPPDPRYSPIGLCSLLTTEMMSRQPRTDLRGQTNPAA\PSAPVPLSCSQNLPVWPSLMAGTTWHSPL\SPSCFWHSPGHN*H*CCVSKD*KSLFWEPTA/YSPLLPSTSP/SSKSMQPPKPRSNADSSVQASLIPRAMSSPTVSPWIMGNGSQGFDHIAVSMWDD

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3913	34281	A	3954	136	420	RESRNLSRGEESEDPAEPS\RNG*EHPLCYLQ*EFLQVLTMLQAEGTMHHFRSICQVNRNFLERGH/SPPSPAPPPETHTGSPRPPSGRSRIRAYLH
3914	34282	A	3955	1	1782	
3915	34283	B	3956	1	3070	
3916	34284	A	3957	104	279	STTHPSVHE/QEEEEEEEEEEEEEEEEEEEEEEEEEEEEERKKECSKAQCKHFPLSEVL
3917	34285	A	3958	1	252	MTVCIHIASEDLPVGRDVEVEDSDIHDRDPGLGDKSETPSE/EKKEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEESNFLQHYLHL
3918	34286	A	3959	2	368	
3919	34287	A	3960	239	432	CLWLFQEEEEEEEEEEEED*EEEEEE/EEEEEEEEEEEEEEEEEEEEEEEEEEEEEKIFLGHRVGI
3920	34288	A	3961	1	577	MQIPSLHKLKKEEEEEEEEEEEEERRRRIGRGREKKEEEEEEEEEEEEEEEEEE\EKKKKEEKKKKEEEEEERRRKKKKERKEEEEEE/GKEEEEGEEGEEEEEEEEEEERRKEEEEEEEEGEEEEEEEEESCLMGPMCVHIHP\DKDLYSLGPPAQRFTGSHAELPT*KARRSSSWTAASRGCAARDPPRRCSPA
3921	34289	A	3962	327	559	PKGRTPSPSCIHRYPCQTPRPHEP*GCHCPEEK/PRPRVWGPSRCMPLGSVQEKRPCPAPGGVQGSFRVSPLMMLTRL
3922	34290	A	3963	1	577	MQIPSLHKLKKEEEEEEEEEEEEERRRRIGRGREKKEEEEEEEEEEEEEEEEEE\EKKKKEEKKKKEEEEEERRRKKKKERKEEEEEE/GKEEEEGEEGEEEEEEEEEEERRKEEEEEEEEGEEEEEEEEESCLMGPMCVHIHP\DKDLYSLGPPAQRFTGSHAELPT*KARRSSSWTAASRGCAARDPPRRCSPA
3923	34291	A	3964	157	272	WCNGSPLYSGW*LVGMESLGRMHKDLWTRQPNQDQDLQ
3924	34292	B	3965	1	3723	
3925	34293	B	3966	1	573	

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3926	34294	A	3967	3	424	AGGQALQGPGQGRGSQGVVG/ PGTGSSGAQHLGKHYPVLSGGS ERSWGRSHTPAGAGC*VRGRR AGGRPGTGHSRPPGGSCLSPAP PNSARWLGLGAPWQAGAGLR DPGDWRRGQGGPGWAWCPGQ PPAQPHTCPPNSTARY
3927	34295	A	3968	3	1238	RGAERRAWSRGPACTRRGPAD WAAAGAGRPCPQRRGVCCTAA VPGAARLSCPTGPGPGDPGRRS LTGQGS*GLGAAFGGWTGALP SWHS*SQGWQTDPVR*VRGTE RDICTGL*QPCPPGGLQTGSGG LEHSLPWPGIGIQAP*GPNHPCR LPRS*ALSAGG\SGGQALQGPG QGRGSQGVVG/PGTGSSGAQH HCCPPYTPPG*HPIPSLLALGPQ SLQPEWAHSGTASGEQHSAGE HGMGTTGH*LPGLCSRCVLGK HYPVLSGGSERSWGRSHTPAG AGC*VRGRRAGGRPGTGHSRPP GGSCLSPAPPNSARWLGLGAP WQAGAGLRDPGDWRRGQGGP GWAWCPGQPPAQPHTCPPAGS LPGAAPGVLCAA*GPAAGV*A GPGPGPGSRR*TRGPSPGAPRPA
3928	34296	A	3969	3	415	ETGRHRSQQSVSSPPVQPRGKR AMYHSAAELVSRGFPRPPVQAP AEPAGAAEGVHSQPASRQEA/G S/TEVRGQAHRFVSPPNAAGAG DG/PDPQSLLAPTNRPCPPGGISP ARSEPVPPAPGRAAP*CFPDLPG LAPPLC
3929	34297	B	3970	1	657	
3930	34298	A	3971	125	524	EAEALENQSQPCDTG/PQSAFSP PGSTQHPRSQLSQCKQRYQDLQ EKLLLSEATVFAQANELEK*RV ILS\GEPLLKQDSKQVQVDLQD LGYETCGQSKNEAEQEETTSPE HEEHSSRKEMVLVEGLCSEQG
3931	34299	A	3972	1	648	MGQVWGLVHFTLEVFHTGDEE EQEYSEVTEDVTEHVYLPAKA KVAKEEEAGIQQARQEGDLEA WQFPVRIHPPDQQENITATFEPF PFKLLKELKQAINQYGPGSPFV MGLLKNVTVSSQMIPTDGDPLT RACLTPAQFLQFKTWWADEAS IQAARNAWAQPQINITADQLLG VGGWAGLDAQFVMQDDAIEQ LRGVCIRAREK\IT*CGEQYPSF

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3932	34300	A	3973	350	1078	GSNRRSNRAEQLRGVCIRAWEK\ITSGEEQYPSFSIVKQGPREPYTDFIAWLQESLKKVIADSAAQDIVLWLLAFDNANPDCQAALRPIRGKAHLVDYIKACDGIRGPAGRLSWLSLQGRPAGAARCTSSSSDWKAQLAPGPHAGPLRCPAFRARQPRLPAVLSAGAAFRDCPLSCVQALLGGSAGPGDRLPGHYSALVALSLPFVKEATMNRWSRNHRSAFFLFSANAHGAEGVLSHTVASR
3933	34301	A	3974	2	630	WDNCGLWFIPSWNLFTLMMRRKESLMK*QKK*QSRFVCQLKLK/PAKEGEVYPYPSAPPPYFEEKEWPDPPDLSFLEDAGQKVIAPVTVQAAPQAIALSSIQAGIQQARREGDLEAWQFPIRIHPPDQQGNIIATFEPFPFKLLKESKQAINQYGQGSPFVMELLKNVAVSSQMIPTDWDALAQACLTLTQFLQFKTLWADEVSIQAACNA
3934	34302	A	3975	264	634	WSSRCQHSSRPQASESWFPG*GPSFWPRIQGDEKTGAGGHP*LGC*PGMTGQGFSTKCQHTCLMWGSHWAQEAPENAPGTSCPGSSGSWVLRSSLQRQKSAWSPG/ASMPAPKMPFLTPSSGFS
3935	34303	A	3976	3	410	KKKVWREEKERLLKMTLEERRKEYLRDYIPLNSILSWKEEMKGQGPK*\EENTQETSQVKKSLTEKVSLYRGDI/L*VDAIVNAANASLLGGGGVDGCIHRAAGPCLLAECRNLNGCDTGHAKITCGYDLPAKCEYN
3936	34304	A	3977	74	432	MLHNLRPRTLTTRTRCPSTPS*TTT*ATPPTTTHGSAGPRAAHLRRTGTRRWRAPRRARSCTRSSPRRARAASTPPLAPARELRSPASPPSCEQSAAPPSGRNGGNFPESIFVKTINSN

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3937	34305	A	3978	2	894	WGGYGMRTGPRTLTTRTRCPS TPS*TTT*ATPPTTTHGSAGPRA RTCAAQRTSGSHPSQRRTSSAA PGV*RANVFPWAH*MKRV*TT LENLTA/PEMAMPPAPHVIFAT DDWAAMVHPSARVPGLDGTG ALLVPTGVCAPGPCKCPLTSSS VTHTRLKTTLSVPPSARQTGRC RSPSDLRCSYPPDEQPVCVPKC GSPWVSVLVAWIQSESAVLDPR HPQHPYLYPVDMQNLLTNLGE PPQARALAAKLLGRPSSSQSGS RVPAVWAQAGNATYITVHTLC SHNTHMSPVRVKRFTHLG
3938	34306	A	3979	157	570	
3939	34307	A	3980	1	936	
3940	34308	B	3981	257	3934	
3941	34309	A	3982	210	4286	MPLKTRTALSDDPDSSTSTLGN MLELPGTSSSSTSQELPFCQPKK KSTPLKYEVGDLIWAKFKRRP WWPCRICSDPLINTHSKMKVSN RRPYRQYYVEAFGDPSERAWV AGKAIVMFEGRHQFEELPVLRR RGKQKEKGYRHKVPQKILSKW EASVGLAEQYDVPKGSKNRKCI PGSI\KLDSEEDMPFEDCTNDPE SEHDLLLNGCLKSLAFDSEHSA DEKEKPCA\KSRARKSSDNPKR T*L*KRATYNFEAH
3942	34310	C	3983	163	309	
3943	34311	A	3984	72	424	RNCGTARSQHEPLGSWLQDTP QPP*TLELAGNLPGD/F*PGPGK EQGMFVCHPIRQPLPRPLPGSSH QSMPTAQPPLSSSSALLPALPAG FPVTQGQWTKLQVQAPAPFHL PPQVEAV*AFYQKQMLVPCSL* SMPTAQPPLSSSSALLPALPAGF PVTQGQWTKLQVQAPAPFHLP PQVEAV
3944	34312	A	3985	1	347	KWQRFVLTGIDTYSRYEFAYPA CHASTKTTIHGLMEFLIHHHGIP HSIASDQGTHLMAKEVRQWAH AHGIHWSYHVPHHPEVAGLIER WNE\GLLKSQLQHQLVNRLRRE LQCWLG
3945	34313	A	3986	1	1716	

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3946	34314	A	3987	1	737	MSSVLLRLIYQLTQKTASFEGGPEQKALQQIQAAVQAALPLGPYDPANPMVLEVSVADRDTVWSLWQVPIGESQLGFWSKALPSSADNYSPFERQLLACYWALVETEYLTMGHEVTMLPELPIMTWVLSDPSSYKPAPMASWGVPYGQLTEEEKTRAWFTDGSARYTETTRKWTAVAIQPLSRTSLKDSNEGKSSHQQAKNGITVLAGVIDPDYQDEISL/LTPQWRCHPGSSVWRASSLGISHPP
3947	34315	A	3988	2	384	CGRSGYWHSSVATKITRLRMLRPREGRKLPPGDIMIPLN*KLRLPPGS/FLLLSHQAKKGVTMLAGVTDPDYQDEISLLLHNGGTGKSPHISDTFYGSKVASCQNTGPEKQDETQAQETAVYKSQIFGS
3948	34316	A	3989	3	1273	
3949	34317	A	3990	3	341	GLGRRQPAGSWPERRPGPSA\RRSTAPRRCGQAES*TERGSQPHQVQGQGRWGVCMKIPSHSGKSPDVSEVSKSRNSIISTAVTHAVVAPEGLKRNGGGSHLRSSRGHRAVIF
3950	34318	A	3991	44	243	
3951	34319	A	3992	40	558	LGSIQVMQAVRNAGSRFLRSWTWPQTAG*QMTAPSSPPPPPGLCSYSCPLSHP/SLPVTVRPWPSPSFSSQQGRGQNA/APGPSAQALDSSKTLRPSRKLNRTRLPATPSSGEPHLDQPSGDPQPLTLARHPPESEPVNFQLCHLLSVGPYANKSEPQPSHLKMRIMLREVVRIT
3952	34320	A	3993	335	581	RRHLFLQWGQRAWRLQVAAAGTTRPTSAMGIRCSEGAAARATAARA*TAGPEPLE/PAANPPPPLTASALRAPPSFVLPQCTR

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3953	34321	A	3994	216	1159	SWHGPPGANTVAAAAGPEE\K AALKLRPTHGWPVRATDVHDV ILKASGESEWRGGSRASHQMSP VAMATALGEGVPVRGPAAGSL RLLPGSSAPLGRDAISSCNGVN GLETTGGRCRHNAPNKRHGDP LLEGAAAR/AQAARA*TAGPEP LE/PAANPPPPLTASALRAPPSF VLPQCTAAPRDPSAAGAAN*G KAQSRNC*NEPFAYGGGTHGT GAGAAVTVAADGN*LGSIQVM QAVRNAGSRFLRSWTWPQTAG PWPSPSF/VFPAGSWPERRPGPS AQALDSSKTLRPSRKLNRTRLP ATPSSAFTLPFQERRAL
3954	34322	A	3995	1	738	MTKRGHGTAWAVASKSASPKP WQLPHSVEPVGTEKSRIEVWEP LPRFQRMYGNTWMSGSSLLQG NQNLHAERYCNSTLERNDTPIE SLKPKRESEDGLGEHNGSTMEE VGAETRVQRHWVRVSMTELAL ASDAHMWGSNPGQRVTGVMV GECGTMLGDTQVLLSNPCGDR ARRAYSTAPDYAVCGNGGKVK LNEQRFGSTNKQGKAAYWME ALRPEPLCWQSNYPEAAAVGK PKAAYTKKLHGEDS*AIPVVTE LGERIAQLLIMLYV\KWGKSEIK RT/G/GFGSTNKQGKAAYWME ALRPEPLCWQSNYPEAAAVGK PKAAYTKKLHGEDS
3955	34323	C	3996	87	329	
3956	34324	A	3997	3	122	
3957	34325	A	3998	1	156	
3958	34326	A	3999	1	353	
3959	34327	A	4000	1	201	
3960	34328	A	4001	56	207	EEKKEKEKEKEKEK/EEEEEEEE EEEEEEEEEEEEEEEEEEEEEE EEEEEEEEEEEEEEEEEEEEEE
3961	34329	A	4002	1	174	MNRC*RHIYSSNEVH*KEEEEE EEEEEEEEEEEEEEEEEEEEEE EEEEEEEEEEEIPLSSL
3962	34330	A	4003	1	278	MTSYKFTEPKNGIWQLHEAAQ LDTTYNKLNKKEEEEEE\EEEEE EEEEEE\EEGEGEEEEEEEEEE EEEEEEEEEEEEEEEEEEEGVIL
3963	34331	A	4004	144	429	DLPREEYALLPAGPRRRCRHTH RYEPNPEFGAKHSCPAA*HRAA PATSDTQE*HRSNAFGEEEEEEE EEEEEEEEEEEEEEEEEEEEEE EEEEEEEEEEEEETLFSNM

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3964	34332	A	4005	3	122	TEEEEEEEEEEEEEEEEEEEEEE EEEEEEEEEEEEEGEEEE\EEEEE
3965	34333	B	4006	1	300	
3966	34334	A	4007	1	1226	MPSSKGVHVHSPPRYLAAKDF KMINKELTAATFMEVIAEDNRF IYDGIDSNFEPELVFLEFFEALLS FAFICVTDQMTKSYTNVPADD VSGNKHETIYTILNQDAQNKSP SAVMSHESDAAHSDSARSSSSK LELSPDVNKIRKSEAMVKEKKK ADKKGEKSARSPSSLSDNLDFS KQDGNTTRQEMSPAGVPLLGM QLNEVKPKKDRQNVQQNEDAT QYEESILTKLIVESYEGEKVRGL YEGEGFAAFQGGCTYRVSCPFE NLQEGEEGRLCEECPDEPRRVH VAGRSMYEGEVVNGMRNGFG MFKCSTQPVSYIGHWCNGKRH GKVGEVATWRAEKKKKEEEEE EEEEEEEE\EEEEEEEEEEEEEE EEEEEEEE\EEEEEEEEEEEEEE EEEEEEEEEEKIRP
3967	34335	A	4008	453	705	LLSIVQAEAVSENSHPILPRVSR SGWGQKEEEEEEE\EEEEEEEEE EEEEEEEEEEEEE\EEEEEEEEE EEEEEEEEEEEEEEGRRRRRSSP SCYSITPELSCKLGHR
3968	34336	A	4009	93	705	ESSTQTCSGFWTGCTALHRWR GMPERCPPESRDS*TRFPQSSLP GHKT/SEKEEEENRKEEEEEEKE KEK/EEEEEEEEEEEEEEEEEEE EEEEKEEEEEEEEEQEEEEDDEE EEEEKSCSVNVSLIELPWDPKA YSRLAPLSSQPGPAVKVPTEHLI AKLEDCVQGFTYLTVEKRWAR AVTGAQELGVDYPRNEKCKPH NNGYDND
3969	34337	A	4010	1	3189	
3970	34338	A	4011	1	5127	
3971	34339	A	4012	209	3816	QGRPTFRFRKYREHHKDTPREE QLQDT*SSDSPKLK*RKKC*GQ PERKVKLPTKGSPSD*KRISRQ/ KTLQARRQSWFFEKINKIDRPQ ARLIKKKREKNQIDTIKNDKGD ITTDPTEIQITIREYYKHLYANK LENLEEMDKFLDTYTLPRLNQE EVESVNRPITGSEIEAITNSLPTK KSPGPDGFTAEFYQRYKEELVP FLLKLFQPIEKEGILPNSFYEASII LIPKPGRDTTKKGNFRPISLMNI DAKIL

SEQ ID NO:	SEQ ID NO: of peptide sequence	Met hod	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
3972	34340	B	4013	1	3570	
3973	34341	A	4014	1	2347	MELKTKARELHDECTSLSSRFD QLEERVSVMEDEMNEMNLPTK KSPGPDGFTAEFYQRYKEELVP FLLKLFQSIEKEGILPNSFYEPSII LIAKPGRDTTKKENFRPISLMNI NAKILNKMLANQIQQHIKKLIH HDQVGFIPGMQGWFNIRKSINV IQHINRTKDKNHMIISIDAEKAF DKIQQHFMLKTLNKLVLEVLA RAIRQEKEIKGIQLGKEEVKVSL FADDMIVYLENPTVSAQNLLKL IGNFSKVSGYKINVQKSQAFLY TNNRQTERQIMSELPFTIASKRI KYLGIQLTRDVKDLFKENNKPL LKEVKEDTNEWKNIPCSWVGRI NIVKMAILPKVIYRFNAIPIKLP MTFFTELEKTTLKFIWNQKRAC IAKSIFSQKNKAGGITLPDFKLY YKATVTKTAWYWYQNRDIAQ WNRTEPSEIMLHIYNYLIFDKPE KNKQWGKDSLFNKWCWENWL AICRKVKLDPFLTPYTKMNSR WIKDLNVRPKTIKTLEENLGITI QDIGVGKDFMSKTPKAMATKA KIDKWDLIKLKSFCTAKETTIRV NRQPTTWEKIFATYSSDKGLISR IYNELKQIYKKKTNNPIKKWAK DVNRHFSKEDIYAAKKHMKKC SSSLAIREMQIKTTMRYHLTPV RMAIIKKSGNNRKIQ/GGIWCD RIL*R*TTCRVAKEIQSL*RRI/W KRLQRTLSIPVLDAV*PPMF*AS
3974	34342	A	4015	1	5073	
3975	34343	A	4016	1	3297	
3976	34344	A	4017	1	3514	MELKTKARELREECRSLRSRCD QLEERVSAMEDEMNEMKREG KFREKRIKRNEQSLQEIWDYVK RPNLRLIGVPESDVENGTKLEN TLQDIIQENFPNLARQANIQIQEI QRTPQRYSLRRATPRHIIVRFTK VEMKEKMLRAAREKDRSTRQK VNKDTQELNSALHQADLIDIYR TLHPKSTEYTFFSAPHHTYSKT DHIVGSKALLSKCKRTEIITNYL SDHSAIKLELRIKNLTKSRSTTW KLNNLLLNDYW

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3977	34345	A	4018	1	2666	MVKGSIQQEELTILNIYAPNTG APRFIKQVLSDLQRDLDSHTLI MEDFNTPLSTLDRSTRQKVNK NTQELNSALHQADLIDIYRTLH PKSTEYTFFSAPHHTYSKIDHIV GSKALLSKCKRTEIITNYLSDHS AIKLELRIKNLTQSRSTTWKLN NLLLNDYWVHNEMKAEIKMFF ETNENKDTTYQNLWDAFKAVC RGKFIALNAYKRKQERSKIDTL TSQLKELEKQEQTHSKASRRQE ITKIRAELKEIETQKTLQKINESR SWFFERINKIDRPLARLIKKKRE KNQIDTIKNDKGDITTDPTEIQT TIRESYKHLYANKLENLEEMDT FLDTYTLPRLNQEEVESLNRPIT GSEIVAIINSLPTKKSPGPDGFTA EFY/PESYL*QTHRQYHTEWAK TASIPFENWHKTGMPSLTTPIQH SVGSSGQGNQPGEGNKGYSIRK RGSQIVPVCRRHDCLSRKPHRL SPKSP*ADKQLQQSLRIQNQCT KITSILIHQQQTNREPNHE*TPIH NCFKENKIPRNPTYKGCEGPLQ GELQTTAQGNKRGHKQMEEHS MLMGRKNQYRENGHTAQGNL QIQCHPHQATNDFLHRIGKNYF KVHMEPKKSPHRQVNPKPKEQ SWRHHTT*LQTILQGYSNQNSM VLVPKQRYRSMEQNRALRNNA AYLQLSDL*QT*EKQAMGKGFP I**MVLGKLASHM*KAETGSLP
3978	34346	A	4019	824	3693	AWKGTTDRSTRQKVNKDTQEL NSALHQADLIDIYRTLHPKSTE YTFF/LAPHHTYSKIDHIVGSKA LLSKCKRTEIITNYLSDHSAIKL ELRIKNFTQSRSTTWKLNNLLL NDYWVHNEMNAEIKMFFETNE NKDTTYQNLWDAFKAVCRGK FIALNAHKRKQERSKIDTLTSQL KELEKQEQTHSKASRRQEITKIR AELKEIETQKTLQKINESRSWFF ERITKSDRPLARLIKKKREKNQI DTIKNDKGDIT
3979	34347	B	4020	1	3765	
3980	34348	A	4021	1	4791	
3981	34349	A	4022	1	3297	

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3982	34350	A	4023	1	3170	MVKGSIQQEELTILNIYAPNTGAPRFIKQVLSDLQRDLDSHTLIMGDFNTPLSTLDRSTRQKVNKDTQELNSALHQADLIDIYRTLHPKSTEYTFFSAPHHTYSKIDHILGSKALLSKCKRIEIITNYLSDHSAIKLELRIKNLTQSRSTTWKLNNLLLNDYWVHNEMKTEIKMFFETNENKDTTYQNLWDAFKAVCRGKFIALNAYKRKEERSKIDTLTSQLKELEKQEQRHSKPSRRQEITKMRAELKEIETQ
3983	34351	A	4024	281	3030	KPRLENYMKNAEASRADAINWKKGY/LVMEDKMNEMKREGKFREKRIKRNKQSLQEIWDYVKRPNLRLISVPESDRENGTKLENTLQDIIQENFPNLARQANIQIQEIQRTPQRYSSRRATPRHIIVRFSKVEMKEKMLRAAREKEIQTNIREYYKHRYANKLENLEEMDKFLNIYTLRRLNQEEVESLNRPIRGSEIVAIINSLPTKKSPGPDGFTAEYYQRYKEELVPFLLKLFQSIEKEGILPNSFYEASII
3984	34352	A	4025	1	3290	MGELITPLSTLDRSTRQKVNKDTQELNSALHQGDLIDIYRTLHPKSTEYTFFSAPHHTYSKIDHILGSKALLSKCKRTEIITNYLSDHSAIKLELRIKNLTQNRSTTWKLNNLLLNDYWIHNEMKAEIKMFFETNENKDTTYQNLWDAFKAVCRGKFIALNAHKRKQERSKIDTLTSQLKELEKQEQTHSKASRRQEITKIRAELKEIETQKTLQKINESRSWFFERINKIDRPLARLIKKKREKNQIDTIKNDK
3985	34353	A	4026	1	3573	
3986	34354	B	4027	1	4251	
3987	34355	B	4028	1	3065	
3988	34356	A	4029	965	4089	TWKGTTSTSRCKIMPKYRSTRQKVNKDTQELNSALHQADLIDIYRTLHTKSTEYTFF/LAPHHTYSKIDHIVGSKALLSKCKRTEIITNYLSDHSAIKLELRIKNLNQSRSTTWKLNNLLLNDYWVHNEMKAEIKMFFETNENKDTTYQNLWDAFKAVCRGKFIALNAHKRKQERSKIDTLTSQLKELEKQEQTHSKASRRQEITKIRAELKEIETQKTLQKINESRSWFFERINKIDRPLARLIKKKREENQID

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3989	34357	A	4030	523	3981	
3990	34358	A	4031	1	3429	
3991	34359	A	4032	1	3156	
3992	34360	A	4033	2	4943	
3993	34361	A	4034	1	6747	
3994	34362	A	4035	1	3928	MAAWNLLLKSYAYWGGLRKEDFHCLDRKTLRTVSFLAALLSYESIGGKGKLTTRKDIYTENPSVHHHHQRPKVDKTTKMGKKQNRKTGNSKMQSASPPPKERSSSPATEQSWMENDFEELREEGFRRSNYSELREDIQTKGKEVENFEKNLEECITRITNTEKCLKELMELKTKARELREECRSLRSRCDQLEERVSAMEDEMNEMKREGKFRDKRIKRNEQSLQEIWDYVKRPNLRLIGVPESDVENGTKLENT
3995	34363	A	4036	1	3638	
3996	34364	A	4037	3	3585	SNSHITILTLNVNGLNAPIKRHRLANWIKSQDPSVCCIQETHLTCRDTHRIKIKGWREIYQANGKQKKAGVAILVSDKTDFKPTKIKRDKEGHYMMVKGSIQQEELTTLNIYAPNTGAPRFIKQVLRDLQRDLDSHTLIMGDFNTPLSTLDRSTRQKVNKDIQDLNSALHQVDLIDIYRTLHPKSTEYTFFSALHHIYSKIDHIVGSKALLSKYKTTEIITNCLSDHSAIKLELRIKKLTQNRSTTWKLNNLLLN
3997	34365	B	4038	877	8907	
3998	34366	A	4039	1	450	QGSPSGSRE*NSQSSAGPQCALPPAMA*VPLSWRSMGKWWKRTSCTSDST*PPSERRHWRSRKSPSAMPASFRCSSASAREMLP*KKGRCAAGSGIAPGPPETWGRTGGCPGKQATCGVSGPNANGEPVL/KYPSSSSEAHGGPGRNGRSD
3999	34367	A	4040	2	522	
4000	34368	B	4041	102	186	
4001	34369	A	4042	2	5417	

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4002	34370	A	4043	45	1585	KQPSGLLKFGNLILKCHPPSLTHMLSQPCA\EAPTPDPNWELA\LYIHPSSGIMSATVSFWSIGTA\YLEAQGIWEP\FRRRLS\FEASNPPFDVGRPFDLRRIVGISSEGNLNTLSCDPGHSRGFCGAGGSSSRPSAGSHKQ*GPSGHPHSSHSNRNSADVDDVRAYNSGRTSSMTSAQAASSQPANKTRPLVLDSNTGAQGHSAGRKSKGAKQSQHGSQHHAHSPLEQHPQPPLPPPVPQPQEPQPERLSPAPLAHPSHPERASSARHSSEDSDITSLIEAMDKDFDHHDSPALEVFTEQPPSPLPKSKGSTEGGPASTFTQAVDGGIQFFTDCWTEGPSSSLLAVAREVQLALCIHELLIHGFSQLQVSGGPGAMPDPAAHLPFFYGSISRAEAEEHLKLAGMADGLFLVRQCLRSLGGYRQLNGTYAIAGGKAHCGPAELCEFYSRDPDGLPCNLRKPCIPPSGLEPQPGSSTACETPWARPRSRPSSARPRRWRSSLLRRTTSGCPGTTAA
4003	34371	A	4044	1	1773	
4004	34372	A	4045	1	663	MALWTLRPTPLLVTCMLICAPGVMGAVVAPLTILGGPLLIRAAWYTAGIVGGLSTVAMCAPSEKFLNMGAPLGVGLGLVFVSSLVDQMGRWFVAGGAAVGLGALCYYGLGLSNEIGAIEKAVEYWFNSFVCHSNQQNACSHELHDERLLGDMGLPILHAMLLRRLPSVDSQNALSSIMLLHTALP*QSAERLFS*TS**EALG*YGFAYPACNASAKTTIRGLTECLIQHHVTPHSIASDQGTHFTAKEVQQWAHAHGIHWPYHVPHHPEAAGL
4005	34373	B	4046	147	330	

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4006	34374	A	4047	485	1568	GEGYKADLAAATVECPICQQQRLTLSPQYSHIPQGDQPTTW*QVDCIGPLPSWEGQRFVLTGIDTYFRYGFAYPACNASVKTTIHGLTECLVHHHGVPHGI\ASVQGTHFMA*EVQQWAHAHGIHWSYHVPHHLEAAGLIEQWNGLLMSQLQHQLGDNTLQGWGKVLQKGVYALNQCSIYGTVSPIARIHGSRNQGVEVAPLKITPSDPLAKCLLPFPKALHSACLEVLVPEGGTLPPGDTTTIPLNWKLRLPPRHFGLLLPLSQKAKKGATVLAGVIDPDYQDEISLLLHIGGKEEYAWNTGDPLGRLLVFPCHVIKVNGKLQQPNPGKTANDPDPSGMKV*VTPPGKKNPRPAEVLAEGK
4007	34375	B	4048	182	662	
4008	34376	A	4049	1	2250	
4009	34377	A	4050	1	1326	
4010	34378	A	4051	1	1614	
4011	34379	A	4052	1	2586	
4012	34380	B	4053	1	1954	
4013	34381	A	4054	1	705	
4014	34382	A	4055	1	1833	
4015	34383	A	4056	1585	4128	
4016	34384	A	4057	1	1425	MARG/NAITLPV/CGRAVKFT/LEVLRGDSVEKTSRVWSGNERDQELLTEDALDDLIPSFLLTGQQTPAFGRRVSGVIEIADGSRRRKAAALTESDYRVLVGELDDEQMAALSRLGNDYRPTSAYERGQRYASRLQNEFAGNISALADAENISHKAHKYFVFEANTGTETGYQGEESLFNKAYYGGGTNFFRKESQKLQQSAKKRDAELANGALGIIELNNDYTLKKVMKPLITSNTVTDEIERANVFKMNGKWDFADFGTTIKQDFRLLGQTSVDRLLQLSQGQAVKGNQLLPVSLVKRKTTLAPNTQTASPRALADSLMQLARQVSRLESGQQSSKQKKAIQTAIRKNKEANAVLARLNSELQQQLKGFADFREPPIKQDFRLLGQTSVDRLLQLSQGQAITELCGAKRVGYFGPTQFYIALKLIAAAQSGLPVRIESIKCGNSYDHDYEFELGTLVLPRSLEGFALSLNCGEHYWL

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4017	34385	A	4058	1461	2496	NKRNHQSVCHAFIRIP\AAPMVDSLIARVGVMARGNAITLPVCGRDVKFTLEVLRGDSVEKTSRVWSGNERDQELLTEDALDDLIPSFLLTGQQTPAFGRRVSGVIEIADGSRRRKAAALTESEGTPAFGRRVSGVIEFADGSRRRKAAALTESDYRVLVGELDDEQMAALSRLGNDYRPTSAYERGQRYASRLQNEFAGNISALADAENISRKIITRCINTAKLPKSVVALFSHPGELSARSGDALQKAFTDKEELLKQQASNLHEQKKAGVIFEAEEVITLLTSVLKTSSASRTSLSSRHQFAPGATVLYKGDKMVLNLDRSRVPTECIEKIEAILKELEKPAP
4018	34386	A	4059	340	2067	
4019	34387	A	4060	1	1959	
4020	34388	A	4061	1	2319	
4021	34389	A	4062	1	1587	
4022	34390	A	4063	964	1757	GYSGSKPDVITLLEQGKEPCVVARDVTRRQCPAAPMVDSLIARVGVMARGNAITLPVCGRDVKFTLEVLRGDSVEKTSRVWSGNERDQELLTEDALDDLIPSFLLTGQQTPAFGRRVSGVIEIADGSRRRKAAALTESDYRVLVGELDDEQMAALSRLGNDYRPTSAYERGQRYASRLQNEFAGNISALADANNISRKNITRCINTAKLPKSVVALFSHPG/ELSARAASQRQQCGYHKLHDKQRLLRG*KGNICAKLLNE
4023	34391	A	4064	1	1554	
4024	34392	B	4065	1	1599	
4025	34393	A	4066	1	682	MKRAPVIPKHTLNTQPVEDTSLSTPAAPMVDSLIARVGVMARGNAITLPVCGRDVKFTLEVLRGDSVEKTSRVWSGNERDQELLTEDALDDLIPSFLLTGQQTPAFGRRVSGVIEIADGSRRRKAAALTESDYRVLVGELDDEQMAALSRLGGATQAFAKENNQK\HTKKRTASLILHAMICCRSLNSSKTKNTKCLNSINQRLKILSLQKDLMCGTAGRCKTLTEQ
4026	34394	A	4067	1	2448	
4027	34395	A	4068	1	2541	
4028	34396	A	4069	1	828	
4029	34397	A	4070	1	1899	
4030	34398	B	4071	1	1686	
4031	34399	A	4072	1	1437	

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4032	34400	A	4073	1	3417	
4033	34401	A	4074	1	3826	
4034	34402	A	4075	812	2578	FIRDFADFGTTIKQDFRLLGQTS VDRLLQLSQGQAVKGNQLLPV SLVKRKTTLAPNTQTASPRALA DSLMQLARQVSRLESGHSNGN GQVSPIFHQTSSSTIRSCSCHLLT LNFLTLQLNTSDIAVFHSTPKLL LVTSTITHMGLNTSQAQSVPVI NSVAGSLAALQPVQFSQQLHSP HQQPLMQQSPGSHMAQQPFMA AVTQLQNSHKFSHRSHGPGQS NDACSEPTNKKMRRNRFKWGP ASQQILYQAYDRQKNPSKEERE ALVEECNRVWQARRLGAFGKE DVHVSFAARRGAKFRHQTLLG RRSSIPAAPMVDSLIARVGVMA RGNAITLPVCGRDVKFTLEVLR GDSVEKTSRVWSGNERDQELL TEDALDDLIPSFLLTGQQTPAFG RRVSGVIEIADGSRRRKAAALT ESDYRVLVGELDDEQMAALSR LGNDYRPTSAYERGQRYASRL QNEFAGNISALADAENISRKIIT RCINTAKLPKSVVALFSHPGELS ARSGDALQKAFTDKEELLKQQ ACKL\HEQKKAGVGDNSIDSW KNAGRVFKDSDKFDANDPILK DQTQEWSGSATFTSDGKIRFIL

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4035	34403	A	4076	1474	3367	REEGANSECLGRHGFKKMLYVKRDEVGKGQIRLETVFEQAIDQRFSTDTSLSTPAAPMVDSLIARVGVMARGNAITLPVCGRDVKFTLEVLRGDSVEKTSRVWSGNERDQELLTEDALDDLIPSF\LLTGHKTPAFGQRVSGVIEIADGSRRRKAAALTESDYRVLVGELDDEQMAALSRLGNDYRPTSAYERGQRYASRLQNEFAGNISALADAENISRKIITRCINTAKLPKSVVALFSHPGE\LSARSGKCMVPTESAPHVTVLGCQCGPLGLENGLKEGYLGRSTLDMEAWQPLQEFYLHNLITGQMFEIAVTQNNSKINSSSPTTEQSWMENDFDELTEVGFRRSVITNFSELKEHVLTHRKEAKNLEKSDGENGTKLENTFQDIIQENFPNLARQVNIQIQEIQKTPQRYSSRRATPGHIIVRFTKVEMKEKVLRAAREKASLAPENLDNSKIRPVVILFHYGESWNLLRADQRLIFAKSWPRASRYQQGHQDLFILRSDLPSQVFIRDKLMERRNRRTGRTEKARIWEVTDRTVRTWIGEAVAAAAADGVTFSVPVTPHTFRHSYAMHMLYAGIPLKVLQSLMGHKSISSTEVYTKVFALDVAARHRVQFAMPESDAVAMLKQLS
4036	34404	A	4077	794	4235	RVSRGRKWFFIALKRMPAMKKAMNLFLGLSNVRTVHPEGFTVYISTHISFPSLSGYRTGLRSFGLVKQKKSPIRMPCVYTNTLCQYRKPDGSGIVSLKIDWIIERYQLPQSYQRMPDFRRRFLQVCVNEINSRTPMRLSYIEKKKGRQTTHIDLALKGLRVLLVEGNDPQGTASMYHGWVPDLHIHAEDTLLPFYLGEKDDVTYAIKPTCWPGLDIIPSCLALHRIETELMGKFDEGKLPTDPHLMLRLAIETVA
4037	34405	A	4078	1	2574	
4038	34406	A	4079	1	536	

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4039	34407	A	4080	368	1449	LKSTNLITFLRLFVPQMPLAYMKFTPSGLVAACAPWLRQRRVVQLGQIAFSAP/YLSQMVRQEMYNRYGESAYEDGYRJYTTITRKVQQAAQQAVRNNVLDYDMRHGYRGPANVLWKVGESAWDNNKITDTLKALPTYGPLLPAAVTSANPQQATAMLADGSTVALSMEGVRWARPYRSDTQQGPTPRKVTDVLQTGQQIWVRQVGDAWWLAQVPEVNSALVSINPQNGAVMALALLNNARPWYLGAQPRDSTIIFCQFGAHPLLDPKTQPVGCRNAARKSCAEIRLVPDARANSGKLVRRYRKYRRQYHKSKSRHQPLRQQQPVRLDWRNVDNQYALTTRFLYQSLQRHAQLNVPLFHVL
4040	34408	A	4081	1420	1842	
4041	34409	A	4082	407	1347	GRJRVHIHKDGRADGGSQPGVTAIQQQLPFAFAFPN*SY*TESAWAQSIK\GPWWLRDQVDGPAGRLAALPQR/SLINAVSTRMEGISGAFNTANPACST*FLCSLLILPSLFSTALPNFRLSAMVSDCTISNMVWST/SAVTDWSCTPLD*ERKHRGTARLTTGKGVGMDRDKQVSTLFLGFCYAHLQWNEDVFIARHVHLHIALFLDQRAQTASYLQYHIFFARFVFPHRTGVFATVARLKHNDNRTIAPCFTRLWTTLRWRHLLFEVAFVVILQQRQQRVLHILCIGRJEVHHQTLFKPGDRRKGKQLRFYVLL
4042	34410	A	4083	1	649	MRHGYPARANVLVKVGESAWDNNKDYRYAKALPTYGPLLPAAVTS/ANPQQATAMLADGSTVA/LSMEGVRWARPYRSDT/QQGPTPRKVTDVLQTGQ/QIWVRQVGDAWWLAQV/PEVNSALVSINPQNGAV/MALVGGFDFNQSKFNRATQALRQAGAHLPAHSQSGHHQQTAR*KSNFCARM*TPDQLSW**KNCPFRLSPT*QRQWSLRRYRPVSQRTSF

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4043	34411	A	4084	2	551	WRAAGPEPCPTGRQLRP/AGDLACSAAAGPGAEPFTAPLALAGRSKCGAAEPAPTQNSRWPMSPHLSLHASPQAEGAGSGL/VPAPRAAAG*RAPQMRP/VVGAEAEEAPGP*EPCRHPAPHASQHRYGCHPS/AAEPCRHPAPHASQHRYGCHPSGLNPAGTQHPMPASTGTAAIHRG*TLPAPSSP
4044	34412	B	4085	1	1029	
4045	34413	A	4086	1	2157	
4046	34414	A	4087	1258	1838	TQVVFITSAWGLGEMVVQGAVNPDEFYVHKPTLAANRPAIVRRTMGSKKIRMVYAPTQEHGKQVKIEDVPQEQRDIFSLTNE\EVQELAQQAVQIEKH\YGSPMD/IEW/AKDG/HTGNGHVQALRNRCPEARQHRMRIPGRILPRPIGRMAGPKTRIEHTSVTVISNRRKIKTENRGHKGYEDRKLHEDLQLRHQS
4047	34415	A	4088	2806	3540	
4048	34416	B	4089	1	1251	
4049	34417	A	4090	341	946	GLSSVGQSVNDHLPWT*GLSSVGQSVNDHLPWT*GLSSVGQSVNDHLPWT*GLSSVGQSINDHLPWA*VLSSVRQSIDDHLPWT*VLSSVRQSIDDHLPWT*GLSSVGQSVDDHLPWT*GLSSVGQSIDDHLPWT*VLSSVRQSIDDHLPWT*GLSSVGQSVDDHLP*M*GLSSVRQ*VT*AKVNPKISAVTRNRGSVESPHLEGRSLKVQVFIPQVEDMSWGPPWLWVEGESWT
4050	34418	A	4091	426	706	VLGGGSEEKAPLWWSGPMVLPGAHSMKT*LPHTHVEFGFACLASAGAQDVGMEGPRHTTENSVTGSPSHFPPRASQHRRGICRPHAGRATADF
4051	34419	A	4092	596	905	GLSSVGQSIDDHLPWT*VLSSVRQSIDDHLPWT*GLSSVGQSVDDHLPWT*GLSSVGQSVDDHLPWT*GLSSVGQSVDDHLPWS*GLSSVGQSVDDHLPWT*GLSSVGQSIDDHLPWA*VLSSVRQSIDDHLPWT*VLSSVRQSIDD/HSSMDVRSV*CRTISR*PSSMDVRAV*CRTINR*PSSMDVSAV*CKTINR*PSSMDVRSV*CRTISR*PS\P*T*GLSMSLIPSQLCGLSAVTPFSAVTRNRGS\ENHPILKAAASRSKSSFPRLKT

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4052	34420	A	4093	3	1194	SLGPRSHSCCRSDYRSGTTVPLVLLPVCGVPALLVFALLSPLCVVCSALCGGLLPVLRASLFLWCVAFLAGLVFVFGFAFFGSLVRGRFLVVVPFFLLFALCRLLFLVCWLRSFGACPVSVCVAGFACFAGLFLVLVSLLSSGFGFRLSFSCVVGSLCLPGFAFRAFCLFFLPCVGPALLAFPGFCGPSSPSLSYGGLFAPWSCALLGFFGCLGWSAPGFLSSFGLSVRVLSLPCASGLRSLSGCALVPGLFLPWVFSPRSLRPLVSFGCLLCSFVSH\NMDWIKES\AGKVIQGNP*WLPVILFFGSVPLTSKAATAKPLMRMG\RALTVSQLT/AVASFAAVYGLFILPT*PTLVGAVQMDDTGTTRIGKLVSNHPFFIRVLLGVALTVCFGFVLGSF
4053	34421	C	4094	70	1950	
4054	34422	B	4095	262	4347	
4055	34423	A	4096	2	458	
4056	34424	A	4097	2	445	QPTERGLCASLKPSRAAIKSQSSKVISFDSMSHIQGTVVQGVGSQGLEQQYRSGVAVFRLHSFSHRLLSACEFSRCRVQAVSRSIILGSGRWQPPSHSSTREWPSGHTVWGLQPHISPLHCPSKDSL*GLCLCNKLPPENLGFSYVL

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4057	34425	A	4098	1	2589	MVWFLKNVNHGTHTNAKKYNDVENKERTGWKWGSTEYLLCARPLRKGNVGLSGDVFLTVFVMKTGHSSSLLPSTTTSDSTAQEGYESRGGMLDWKHLLDSPDSTDPLGAVSSHNHQDKKAMLKDGEERPFNEPGVFHLLADHQLTQKVASIPGSAVCAYDMLDIASVFTGRFKEQKSPDSTWTPVPDERVPKPRPGCCAGSSSLERYATSNEFPDDTLNFIKTHPLMDEAVPSIFNRPWFLRTMVRYRLTKIAVDTAAGPYQNHTVVFLGSEKGIILKFLARIGNSGFLNDSLFLEEMSVYNSEKKWSTAKPVRVTIILNPGQASFCITLRETV/C*RRKHIWCPPYRCTLQ*HFCPCH\CLSGKETLCRVTGGMKVKADRDESLPYAAMLAAQDMAQRCKELGITALHIKHRATGGNRTKTPGPGA\SRPSSPCPLGCLK/WQTLFPRRRLRWPQGGRRKRSQLEAQRVIRESYLKGHDQLVPVTLLAIAVILAFVMGAVFSGITVYCVCDHRRKDVAVVQRKEKELTHSRRGSMSSVTKLSGLFGDTQSKDPKPEAILTPLMHNGKLATPGNTAKMLIKADQHHLDLTALPTPESTPTLQQKRKPSRGSREWERNQNLINACTKDMPPMGSPVIPTDLPLRASPSHIPSVVVLPITQQGYQHEYVDQPKMSEVAQMALEDQAATLEYKTIKEHLSSK
4058	34426	B	4099	1	1299	
4059	34427	A	4100	95	502	FPEIPQSCREGAPGPAKPGGPRAREPCPNRTAASWGVHCEDGGSTVRTGGPL*GRGVHREDGASSPQHPPRRGRGLGHLGPRPL*GQGDAAAAPGHRGKS/GGKGFLPALRVQRGERGRVSRRAVCMWTSLCASVPS
4060	34428	A	4101	2	653	DSFGSMSVLIKNPRTLFGGKPYVCRECGRGFTWKSNLITHQRTHSGEKPYVCKDCGRGFTWKSNLFTHQRTHSGLKLYVCKECGQSFSLKSNLITHQRAHTGEKPYVCRECGRGFRQHSHLVRHKRTHSGEKPYICRECEQGFSQKSHLIRHLRTHTGEKPYVCTECGRHFSWKSNLKTHQRTHSGVKPYVCLECGQCFSLKSNLNKHQ\RSHTGEK

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4061	34429	A	4102	8	389	LPASASQSVGTTGVISFENTCNICHFFFLLLLFFSSSSSFFFLPFSFSFRVSLF*IQPLKTTASTVQGRQHSGGYRASPERRADQRAHTGEKP/YVCRECGRGFRQHSHLQLSVYPHSFWTQDKRSNH
4062	34430	A	4103	1	740	EGKRGRPFRIPRPAHPFPHELQSRLCILKPLHHPTPSSCPSS*TPVAPLPSHPCAPH/SARSCPVSDEAAL\P*SMALWARAGLLEAPTTLLPAAPDASSPA/MPPSRKLPPPLPL/CPEPLGPSPAAPSPPAPPGPNAAARPPL/PPSPSAAPGPRRPGA\RPVGPSRGPG/PRNSRSLRAPDVHTAPMRCLPSVRPPLPVLSAL/PDPLPRPPSFVPSLPSP/PSSGPSCPPTSAPPGSPRPGFVRLPCLLFWGS
4063	34431	B	4104	48	272	
4064	34432	A	4105	2	622	CPLSPLLFNIVLELLARAIRKEK*/LKGIQIGEEEVKLSLFGDDLIVYLENPKYSSKKLLELVNEFNKVSGYKIYVHKSVALLYTNSDQAENQIKNSTPFTTATSSSSSSSSSPQGIFLTKRLKNF*RGKFKTLVKKNQGDPKKGKNPPGPKMGKNNFGKTPFWAKKI*KFHSI\PKKTPPFFFQKLKKTGVKFFWAPKGPKGFLSKK
4065	34433	A	4106	39	1043	QKQPVWQRCREIGTLGYCGWKWTLDIHGRGHRILSGGVEIPGPWTEGFIQGRDVGELQEPGLSGRESIH*\GKSYEYECSEDGEVFRVRASLTNHQVIHTAEKPYKCTECGKVFSRNSHLVEHWRIHTGQKPYKCSECDKVFNRNSNLARHQRIHTGEKPHKCNECGKAFRECSGLTTHLVIHTGEKPYKCNECGKNFRHKFSLTNHQRSHTAEKPYKCNECGKVFSLLSYLARHQIIHSTEKPYKCNECGRAFHKRPGLMAHLLIHTGEKPYKCNECDKVFGRKF\NLTNHQRIHTGERPYKCNACGKVFNQNPHLSRHRKIHAGENSLRTLQME

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4066	34434	A	4107	3	941	QQHQQQQHFVGQVAIQQQQQ QGPGVQTNQALGPKPQGLMPP SSHQDLLVQQVSPRPPQGPQG MVGPAQVGVLQHQLHGALGP QGLH*QVFMP\QSRVFSSPQLA QQGQGLMGHRLVTAQQQQQQ QQHQQQGSMAGLSHLQQSLMS HSGQPKLSAQPMCSLLQLLQQ QQLLS*QQHLQQQQQQQLQQQ QQL*QPQLHQQQQQQQLQQQQ PQQL\QQQHQQLQQPQINSQ/HL FPSRRPPNHMGLLTHSPNLTAS LRLTSTHKAALGPGLQAALGHP KDGLLWKTLGTWRARGLICTG GIISYFTQHSWEVKVFTTL
4067	34435	A	4108	1	2255	MEKNKVVKREAEANSINLSVY EPFKVRKAEDKLKENSDNVLE NRVLDGKLSSEKNDTCLPGTAP SKTKSSSKLSSCSSAIMALSAKK AASDSCKEPVANSRESSPLPKE VNDSQARAPLQSTVMTNAVSP AELTPKQVTIKPVATAFLPVSA VNEMKTAGSRVINLKLANNTT VKATVISAASVQSASSAIIKAAN AIQQQTVVVPAPSRANAKLVPK TVHLANINLLPQGAQATSELRQ VLTKAQQQIKQAIINAAASQPP KKVSRVQVVSSLQSSVVEAFN KVLSSVNPVPVYIPNLSPPTNAG ITLPTRGYKCLECGDSFAVEKS LTQHYDRQSMRIEVTCNHGTK NLIFYNKCSLLSHARGHKEKGV AADTRGQKTCTICQMLLPNQCS YASHQRIHQHKSLYTCPECGAI CRSVHFQTHVTKNCLHYMRRV GFRCVHCNVVYSDVAALQSHI QGSHCEVFYKCPICPMACKSAP STHSHTYTQHPGIKIGEPEIIYKC SMCDTVFTLQTLLYRHFDQHIE NQKLSVFKCPDCYLLYAQKQL MMDHIKSMHGTLKSIEGPPNLG INLPLSIKPATQNSANQNKEDT KSMNGKEKLEKKSPSPVKKSV ETKKVASPGWTCWECDRLFIQ RDVYISHVRKEQGKQMKKHPC RHLCQHNRIKHKGIRKVYACSH CPDSRRTFTKRLMLEKHVQLM
4068	34436	B	4109	1	411	
4069	34437	C	4110	54	146	
4070	34438	A	4111	1	1937	

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4071	34439	A	4112	1	1830	MCIEVTCNHCTKNLIVYNKCNL LSQARGHKEKGVVMQCSYSIL KPVSAGHIIVSPSSNSSSSSSTLQ SPVGTGIHTVTKIQSGITGTVISA PSSTPSTTAMPLDEDPSKLCRH NLKCLKCNEIFQDKRSLATHFQ QAADMSGQKTCTICQMLLPNQ/ CQRIHQHKSPYTCPECRAICRK KRT\QIHEWERETGKEISISFEKK SMETKKVASPGWTCWECDHLF MQRDVYISHLRKEHGKQMKK HPCRQCDKPFSSSHRLCWHNRI KHKGIRKVYACSHCPDSTGTFT KGLMLEKHV\H*CMASRTLT*K K*QTPPMRRKQK*K*TSRSAVP SG\VERTGSGVQASQRSNNSTT EKAENQCF*GSQAPLCCTQVKG TSASAQAKWGWRR*PTGEQTQ PRGRISQW\VMSDRKCKVCAKT FETKAALNTHMQTHGHAEGCL KQPCRSLLSQPRIKTEARNLIRN ADFLNSILRNGEGYSKEKKNGT GFLGRSARLALGAQGGKSWRF LFWVLLPNVLVLRVGMHDVN HRLINAAGCVSQLAVTLSTEPH GISSAISRVPRHCHPSGENSMAT SLNVNRSISRLAAGSGVLAMDL PIPAGHRAIETGLLGTEDTEQ
4072	34440	C	4113	217	510	
4073	34441	A	4114	210	281	
4074	34442	A	4115	1	675	
4075	34443	C	4116	126	434	
4076	34444	A	4117	804	2061	WERREAGGEDEGINIHEP*VEE EMKKHESNNVGLLENLTNGVT AGNGDNGLIPQRKSRTPENQQF PDNESEEYHSLGDKSKTSFQNS NNNNNKQQEQQQNPTFSNTR KLTKLYKAPIPPSIILSGCPNIND SNWQEIEHGMQTAGLPTRPLSH GLQQKGAAFRCLGCKCSEPFTG SLILQKAKTNTQKWQATYPKS QNEQLVPSVGKSYRCSTPAQP MKTAVGHKPCKATGAELPKAL GAQPLHPCALDVGQGFKKGNF GAVGLNGLLGLEFHGVSGVLL VGPGDGGLISEGVVREDLMCG VWSAGTWSVGTAERCLEKPGA LHVIEGPLDSWDGPVMPNGPV KSRQSSCLDGPGRCCSEILTGQS HGNKKPARASSKSSQSINDRPL AVLTNQYQCEQLASERQPSSNS

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4077	34445	A	4118	1	357	GKLMLPGSTRKPQVPVDRKMG HEGVFVWQAGLRARPGPSLPFS HGLTLHLHWPLALPV/GATSSP CEAGDLGV\PLAAGTWCPWEA *RQEEAGWQAPGRAGPARVG WGGTGLTSAEVIITI
4078	34446	A	4119	1	771	MLISHKQLSPQLLSLTLPLSEGK AGWAGECPNPPSKDSPVQGIG/ GPPP/GYQKCR*DTASMLTMAP CHGPVCPPHPGWRPRSGSRVIL PAPPGHHPWP\GPRARNGLGTF QGCSTGWQVQETCFGPGGWLG DRHLVGPAATGARCLPAARGP/ DGALHPAVPTGKLKGQP\GPGA RHQRTYD*LPRPCGAAGLGSPP A*HPISEETENQWGLHGPPQPA WARPDHGCQ/APTLSPSLKRKP GRVTAGGPMPGCFSTSSVPTT
4079	34447	A	4120	1	402	MLISHKQLSPQLLSLTLPLSEGK AGWAGECPNPPSKDSPVQGIGD LHQLPKMQIRYSIHADDGSVPR AAHKRGLRKRTLKTISLPRQES AFPFHGQGGDPGVVPGSSFLHP LGTTPGQGPRARNGLG\PSRAA PPAGRGVAGGSPSGG\PAATGA RCLPAARGPVGPYTQQSQRAS* KGSLGPGARHQRTYD*LPRPCG AAGLGSPPA*HPISEETENQWG LHGPPQPAWARPDHGRQPLRC HPP*RGSQGGPQKAAVSQQIPR AGQEGTH*DPTEWGPPDGDQG GPRESCRGLQGGRGQCLCDWS PNTSEI*YPHA*NGD*KAG\PPM DTKSQLQVSTPKSPASHGEDVA RLEEPEASGD/RSVP\GLPGASLI PIWRPPFSRISVRTFLPSPWNLL RDCGFLGTSLASSSGRVTA
4080	34448	C	4121	111	218	
4081	34449	A	4122	2	453	WWPVLSVPPECRLPGRLPSG*V RGPAPWWPEPASQDKSQLSSR GFPGKVSLGKGMAFSPLQTAP* KWLGLSPPLSSTENTASRGHTS PSSRNGFDSQPRDSRTGRECQA TQLPAQHSHAEVLHFGGAMSG QLSLVGPQDSKRTARLTDSQ

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4082	34450	A	4123	1146	1775	KGWLEGAPEA*ERYPG\PPCVVCSLSDAPWVGHPAPSLGV*EPNPP*SRGESQGPTSSICRQSSGDLG*KLESPIHTVIPRHTSQARQGHTAPFPPFQVPS*LLV*LKAVSLAPAEAP*PASGLHAPWPVAPRVTCAI/PAKGTTVPAGPAELRPVSPPPILLP/PDSRSSAFPSRKGPASPYETCSPPTS*/EVPS*TYKSMGPGIRLPALPASPRVPSEGPGLSEHPEGPPALPPAIPFS\SPSWFKQCSFSIRPGWLLHGAPQGKGWPQASWVGKTG*PEKRGSPRGPEHSALNLRVALPGVAV*EGPACVGWGGPPQPPGAICEATAPPSI/VPPLSLPAPFPGTLP/PPTPAASP/PPALPPLLRRGRPRPCAALALPALSSLFS/PPVFSLLSLQLPADRVRQVHPVLRAPGPPFRPPKQIPPSSSGDLPFPSLPGR/PVL*LEKWLPPAPKASPPSSVNLILLVVVKLNTFRCGPLVKNLVPPSVVCPCPCSYKYL*ILIYIHTLHMGQPPSPSSAGNQSLCYPCGGLVAQPTKRTLVPPTIQLQSVPPPV/KPPCHARPVDSQPPPSLPPPTKHGGAVQAAVWPDSFYPVLLSLG
4083	34451	A	4124	146	1701	TFLGYLETAHGPSAQQCPTGLFAFRSLGRGLLLTSLPKQPARSPPREDVPRSTTQEMTRPRHPPRKPAQPGLGARRRGAPV/RGLSKSRELNSGNTSDSGNSFT\PPHPRTRGPCWRISPPPAGAESQGDAMLLARMCQMPSLGLMSRTFPHSSTGKARGFQSPCLECAEVKKSSLVPSTARSSPMKGCSRSSSYASTRSSSHSSQSPNPRASPRVRTHTCIL*TRKRPRETKSSAKVT\HYYSSKSGKRSPPSRSSRSRRSPSYSRYSPSSPNSPADIPQNSHPQPSASTDRPHIQSPQFLPTHQGLRNIHVLTPAAPALL*CPPANADTPAQAQPPPLRY*QPSQTLTAAPSSSLRSPLRQRADPIP*PSGGAGSQIQ\WKDSQQRERERARRRRRSYSPMRKRRRDSPSHLEARRITSARKRPIPYYRPSPSSSGSLSSTSSWYSSSSSRSASRSYSRSRSRSRSRRRSRTRTSSSSSSRSPSPGSRSRSRSRSRSRSRSRSQSRSYSSADSYSSTRR

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4084	34452	A	4125	1	1068	MLLLELNAPEHVLETINFQTLT AFCNTFHILRPTKAPGFVYAWL ELISHRIFIARMLAHTPQQKGW PMYAQLLIDLFKYLAPFLRNVE LTKPMQILYKGTLRVLLVLLHD FPEFLCDYHYGFCDVIPPNCIQL RNLILSAFPRNMRLPDPFTPNLK VDMLSEINIAPRILTNFTGVMPP QFKKDLDSYLKTRSPVTFLSDL RSN\LQVSNEPGNRYNLQLINA LVLYVGTQAIAHIHNKGSTPSM STITHSAHMDIFQNLAVDLDTE GRYLFLNAIANQ\LRYPNSHTH YFSCTML\YLFGRRANSGRPFQ\ EQITRVLLERLIVNRPHPWGLLI TFIELIKNPAFKFWNHEFVHCAP
4085	34453	A	4126	1	984	MQANLEMAGNGVTSMGMEPL AIPHIYCCSEGTCNFSNTENHCL RAALSMLLNGTPFAFVIDLAAL ASRREYLKLDKWLTDKIREHGP SVHGLFPSRVLSPALGPGAFPG RHNCGSCVAPQSGLPGVHPVEL PWSISKLFRLRSPANFSDVLGSR SKVLLLMCTLKYCGMQLGADA TRVDMLTFLPTLGFIRNNDYTD DTKASELTELSHNLHAYDSVTG VPGDETECSKTVSTWAYTAESL QGYMAAKLLGRNLTVPSRYLF LNAIANQLRYPNSHTHYFSCTM LYLFAEANTEAIQEQIT/RLVRE RI*S*ANAYWHSEKFYQFTCEL
4086	34454	C	4127	1	399	
4087	34455	A	4128	1	868	MANVCNPSTLGGRGGRITRRPE DPGSPVYSVPPASYHPKPWLGA QPATVVTPGVNVTLRCRAPQP AWRFGLFKPGEIAPLLFRDVSS ELAEFFLEEVTPAQGGIYRCCY RRPDWGPGVWSQPSDVLELLV TEELPRPSLVALPGPVVGPGAN VSLRCAGRLRNMSFVLYREGV AAPLQYRHSAQPWADFTLLGA RAPGTYSCYYHTPSAPYVLSQR SEVLVISWE\TLAPPTTPGGT*S AWGWPGWSSSPWARWSLLTG AVRTALLLFPQVPHRATTPWVT SYDWVWLP
4088	34456	A	4129	1	270	
4089	34457	B	4130	39	919	

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4090	34458	A	4131	3	466	GRALCPPRLLAAGRVLGPGRRSPG\PGPGVP/GG*R*GGAEPRPGAPRGRVLPPSAGSGQFSAATPAQNGLPALRGPGSRPGIRSKAVRPVPLGRVGVYFRDALRASGQSGRKLCCIGNTLSPTSFSVGKEVPRKHETNQKHEKGILCMEAVKP
4091	34459	A	4132	1	1647	MWRWLYAGARMTVRDKQPLEQMLAGCTHASLVPTQLWRLLVNRSSVSLKAVLLGGAAIPVELTEQARDMGIRCFCGYGLTEFASTVCAKEADGLADVGSPLPGREVKIVNNEVWLRAASMAEGYWRNGQLVSLVNDEGWYATRDRREMHNGKLTIVGRLDNLFFSGGEGIQPEEVERVIAAHPAVLQVFIVPVADKEFCHRPVAVMEYDHESVDLSEWVKDKLARFQHLVRWLTLPAEPKNGGIKFHVSAKRVGALTTRMEAAQQHADDKIRQMINSEQRLSEQFENLANRIFEHSNRRVDEQNRQSLNSLLSPLREQLDGFRRQFRTASLMKVAGWDYLMNSLYNANSSALVNRVRYKWIAAFEGGFTGIVATLDTGRPGPVMAFRVDMDALDLSEEQDVSHRPYRDGFASCNAGMMHACGHDGHTAIGLGLAHTLKQFESGLHGVIKLIFQPAEE\VRVARGRWSMQVS*MMLIILLPCTLALAYLRALLCAAVIILWQPPNLTRTSPVPPLTQAQNQKTVTMPCWRHTSHSCTACNRPAQRRSFQS
4092	34460	A	4133	864	1128	TGRSTIRRQRREPRRKAATLRFDRNGCRARCTPP\GRKEQRYQQTADGDKGAEFYRRPEGVEIVAVMEQRDEVIQADKLAGETKRIDAL
4093	34461	A	4134	618	1102	HSNAAPTARSSFVQNTPSSCGYSRRAWRISSIPEETDRTSYRNIQCGNHPPVPARLPAGQTGDGDIPPRPRWQSPQTAPRKPPDLP/LIRKNKIPMFRSATTQPGLTGTIAKASSSEVKAIIGARVKMTRSENFGIQSSLKNILIMSATSWSEPPQPTRLGP

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4094	34462	A	4135	2400	3201	VGGGRNRSPGVACWVEDGNGDAVRDGW\ALDADWQASQAMRRKQQPE\YWQHDAATADADRQMNMPV\LH\RALVAGRAQEMNGAQGKTLLKGW\DEASARRGT\KTED\FCEEDTRDDAMIAWMPR*PGVLPRADAWANVLNHGVGWKKAQLK\STWM\PQVQQ*WRGD\KAANSNAAVAHTVVLLNSGGDATQ/TAAFPISSPLSV/EEVCVTMVIA*FWMWDSGSGGVVLCSSSGRSLTSWSATKVRG/SGHKGRWCSRQGVTCQVRHGGHVAPH
4095	34463	A	4136	118	1008	
4096	34464	A	4137	3	1140	KHTYMLSILKPVRTSALPPPAPAQTLCTQLSRVSSRLL*DHPSRWGLR/PSTGMSQARACSPGSLGWMQRSSFTPGAGRVRHIPN\SAGSTRRPACGSRSAAAPVRPCRRTR*G/RSSVVERFMTALSLACRALPGP*AAPGPSITRRFTISAELKDTRL/PREHVVPLVCTHAIAVPDRGAAVRPTRRRDAAAPPSPLVGDVTLQCPSQ*RGSNAPDQVRLPCVG*RPRSSLQRSGLSVFSADGSTSGPEPASGRKDAGWPARVLRFGTLSRGAPEAGADWGPYSPGSPGAAASGAPWLGQPQALQGAGGQLVGSENGERGTGTKPRVSVSVAYGEIALPADTSWSSRAGAAVLLGLSRSTGGEGPGNMGHGGQSQMLTLEVL
4097	34465	A	4138	10	585	PLEMELNLISIEVWGERLGISTGTEKMPTLKHRTWPVECSKASSLEGDLRSL/S*LEVISAFSADPASADDSPGCWKKKDDCSMVHLHRQEWQQQQCCQ*K*RKQPPGERRNKCGSHPVCGTVLWQP*QTH\QISSCPTVGCPPSHSSFSILDGANAGQEKQSTTEPEPALFLLPPSRGAFGPFGLLSDLRRQL
4098	34466	A	4139	1	474	
4099	34467	A	4140	458	612	ASCMASVDISVLTCMWRCTIEQSSSFLCLLTPLWE*SWCHVTRICPFISLG

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4100	34468	A	4141	1	829	MGRPDLILSSILGLRWLLLPQSSRAGRRGAIREASDAEQVTFSGGTVPARTSSGREWRSLLGPDMETTSLFCIDTKTTFLFVYRYGDHIPLVPEQSGLEPLLIWADPGLFHVRLFHLLTIDDNFCGLDMNAPLGVSDMVRGIPVFTEDRDRMTSVIAYVYKNHSLAFVGTKSGKLKK/VRSSAAP*VWDQDTPRSLGQQGAQRQP/ILRQCVYTFFQLN*RCPHSTARRELRTGGFIPTRSHQDGLRSAARCTQGTTQ*ASWSCVHVCASVRAMCSYC
4101	34469	A	4142	5	237	NFGAMTRIR\DLPWEINPLSSCSSLCEKDPPTTSSPQTN*PKEHHTNFQSETGDEFYPWTQNFSTGHGLGKTVFPWCL
4102	34470	A	4143	1125	1190	
4103	34471	A	4144	306	573	RNFGAMTRIR\DLPWEINPLSSCSLLREKDPPTTSGPQTNQPKKHLTNFKSGKRPLLTLFSNLSHCPSTTFFFPFFNLSLLLISIPFIFW
4104	34472	A	4145	1	329	ASHSWQTLQHSGRYSRSSG/SAGSPRDCAARAPTISPGCAMAWLNLDSISPSSQSKASPLSQLTCPETSYTGCP*SAPHSPPPPWCPQERCACKGHCLHHRDGCCGYGYN
4105	34473	A	4146	2	336	SILTRKCKYGMEIPT/NIPGLGAAGPTGMFFGSAPSPMGGISPAMTPWNQGATPAYGAWSPSVGSGMTPGAAGFSPPKA/PTYSPTSPGYSPTSPTYSLTSPAISPDDSDEE
4106	34474	B	4147	1	1260	
4107	34475	A	4148	150	335	SFQQSAPW*ASGQSCASDPAPPATARGRFGPHQSQAFHSRHSPIPDPLPPPCSGGWGHSRW
4108	34476	B	4149	1	3267	

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4109	34477	A	4150	1528	2973	GKQIFSLIIPGHINCIRTHSTHPD DEDSGPYKHISPGDTKTVINNW LLIEGHTIGIGDSIADSKTYQDIQ NTIKKAKQDVIEVIEKAHNNEL EPTPGNTLRQTFENQVIAVVGQ QNVEGKRIP*LPPPL*WGAGRR EGVG*CGRFSEHSRSSAAGYRG GRPCC\PSWEDDP/GAPPDPPAS AQIPAPTRSGCVRCSARPSPGPP AECAAGPSHWYNQSGTSSQKP CWKA*AYPGSGTQRSRGSQAR SHP**SEAESGA*SQMESACPRR SAVQRQQ*PDSQTSAAECSLG WAPAHCCVPSR*PLLRPAWPS* *CSECPGKS*NQQWSPQCQ*YD PNPQSTVVAEDQEWVNVYYE MPDFDVARISPWLLRVELDRK HMTDRKLTMEQIAEKINAGFG DDLNCIFNDDNAEKLVLRIRIM NSDENKMQEVMGVLEVSVSHV
4110	34478	A	4151	459	940	HLPGGGVPGREGGSPDQHVAP GAVSGGAGGGSTRGRGSRRRR PGRPRPGPRQPRRGALPGGEHG LRASARCAARAQQRDPG/TPSC SSWACPTPRRPWAPAASSRLRR PPRGPACATPPPCRPPARRTCTG RCPPSCCLCGSPTTWRRPPPTG GALESPKRR
4111	34479	A	4152	264	1386	SSRCQPVCESGHPGYGQSPA/YT TAGRTESGGTGST/GDNHPLWP CI/GGAPCPAQNTPHLRCV*RSH ALALDSAGSSSPESPH*RASIPH TTLGQKRRSWAGTAHS\PMAPC AAASISTST*LSHHHSPAAQSVC PSSHTTPSFCPIQKFHCFR/SPQR NTS*VVLCPGG*LRVG*WPSSG HDRSWYHTREPSVGN*HRSHQ RR*RGTAPAPGPSARLQCPARG SRSSHSAPASSSRRPFPGSTPAG LGFPSARFPVGKPVVPAALMNR PTRGERRFAYWAPGWFFFSPVR RATADCPSP/SWP*ESCSKRSTL VCPSRRKSCLMVVPKSAKSPVL AK/YGPVGHDHGTEHDVVLGE VQGKRPVAPTMGTPKHKAVHP RAPH
4112	34480	B	4153	52	363	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
4113	34481	A	4154	321	802	HLPGGGVPGREGGSPDQHVAPGAVSGGAGGGSTRGRGSRRRRPGRPRPGPRQPRRGALPGGEHGLRASARCAARAQQRDPG/TPSCSSWACPTPRRPWAPAASSRLRRPPRGPACATPPPCRPPARRTCTGRCPPSCCLCGSPTTWRRPPPTGGALESPKRR
4114	34482	A	4155	15	263	CGRFSEHSRSSAAGYRGGRPCC\PSWEDDP/GAPPDPPASAQIPAPTRSGCVRCSARPSPGPPAECAAGPSHWYNQSGTWKCKG
4115	34483	A	4156	3	518	SPSVGSGMTPGAAGFSPSAASDASGFSPGYSPAWSPKPGVPGVPQVPSKPLKSLHPGGVVRHLSGQVCFLHSSG*VCPLLISFVGCFPTGGAMSPSYSPTSPA\YEPRSPGGYTPQSPSYSPTSPSYSPTSPSYSPTSPNYSPTSPSYSPTSPSYSPTSGSYSPTSPSYSPT
4116	34484	B	4157	620	6763	
4117	34485	C	4158	430	870	
4118	34486	A	4159	1	3039	MDSETRRTAKVRLLMTVLRDQDRVSGVQAHPEQFQQAICPLCGVSLTRSGTTFGSPSEIYSPLGESRASSGLPRRDGRLIGEEPPEKKFSRSPKGD/LSSGGQRIDYRVCVPTKFNL*VLSF*PRGQGAGGQSPGFSVRRLLVLVWSSGTFV*NGK*QKLL*TLCECVHD*GVQGPASGSPVCSSTAKATEFEKDPSGPFSSSSLPLTPYISFSRVTASSASPGLGSALTPQTLKRKGRI*AICL*VVETPKVFR
4119	34487	A	4160	1	772	MVARAFLWSQVIRRLGRKGGLSQGDRGCNTALAEGRLDPDLTRGHPALCLPRRPAPRPAEVRREGEAEQPEAGQPPGAAPRRARDNGAAAAAAGGRLLQSVRPAVVCPHPGPQASYGLRYIAKVLKNSIHEKFPDATEDELLKIVGNLLYYRYMNPAIVAPDGFDIID\MTAGGQNNSDQRKNLRSTAKVLQHAASNKLFEGENEHLSSMNNYLSETYQEFRFKNVTFDIIATEDVGIFDVRSKFLGVEMEKVQLNIQ
4120	34488	A	4161	174	444	YHRHDSWRNTRR*\IKLDGKGEPKGAEESEATSKYTAAKLHEKGVLLDIDDLQTNQNAVNDFSVGPQDEVIVEDITNCYLCEIFKRYEWVT

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4121	34489	A	4162	379	520	GTSHRGASQRRCCPPLSKTGPKTPCGKGAPSAP*QGGLDVQGEPGGK\GDSSGECVGGNVAGLHKGGGTRADSQVPGGMRGGRMSY/GG/HLTAEGPMGRSGPR/GAVPSLYPPGFSRGSCSRQYSGAHMPILTGHVGWSESSLDPPRAGQDRFLGTARP*GTSHRGASQRRCCPPLSKTGPKTPCGKGAPSAPFIPAGPTFDHKALM
4122	34490	A	4163	455	798	
4123	34491	A	4164	32	2109	WIGGCPGSQPDATAIMGWTLAPHSSRCHRCCHYRCHCRCCLCPAEMTVGRPEGAPGGAEGSRQIFPPESFADTEAGEELSGDGLVLPRASKLDEVLSPQEEIDPTSDSTGSIYHTLLDLAQKGRWLSVWSLSFSLTQRVMKTSLKMRRTWRVSSKTRTGGWCRSSARRL*GVAPQGAA/DSLNNLPSNIPRPQTQPPSGSRPPSQHRSVSSWASSITVPRPFRMTLREARKKAEWLGSPASFEQERQRAQRQGEEEAECHRQFRAQPVPAHVYLPLYQEIMERSEARRQAGIQKRKELLLSSLKPFSFLEKEEQLKEAARQRDLAATAEAKISKQKATRRIPKSILEPALGDKLQEAELFRKIRIQMRALDMLQMASSPIASSSNRANPQPRTATRTQQEKLGFLHTNFRFQPRVNPVVPDYEGLYKAFQRRAAKRRETQEATRNKPFLLRTANLRHPQRPCDAATTGRRQDSPQPPATPLPRSRSLSGLASLSANTLPVHITDATRKRESAVRSALEKKNKADESIQWLEIHKKKSQAMSKSVTLRAKAMDPHKSLEEVFKAKLKENRNNDRKRAKEYKKELEEMKQRIQTRPYLFEQVAKDLAKKEAEQWYLDTLKQAG\RRKTL*ETRVKAPGLFKRKRPKSRIFPGSKKLQNSASEIQSR/RLEGSLEQPASPRKVLEELSHQSPENLVSLA
4124	34492	A	4165	251	637	

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4125	34493	A	4166	1	1344	PGRTTRSMAEDVFLSAPIPRGC ADGRDADPTEEHMAQTERNDE EQFECQELL*CHVQVGAPEEEE EEEEDAVLVAEAEAVAAGWM LNFLCLSLCRAFREGRSEDFRRT RNSAEAIIHGLCSLTACQLRTIYI CQFLTRIAAGKTLDAQFENDER ITPLESALMIWGSIEKEHDKLHE EIQNLIKIQAIAVCMENGNFKG AEEVFERIFGDPNS\HMPFKSKL LMIISQKDTFHSFF\QHFSYNHM MEKIKSYV\NYVLSEKSSTFLM KAAAKVVESKRTRTITSQDKPS GNDVEMETEANLGYKKKC*LT NSLR*LNPQRVQYPY*GSHKNL FLSKLQHGTQQQDLNKKERRV GTPQSTKKKKESRRATESRIPVS KSQPVTPEKHRARKRQAWLWE EDKNLRSGVRKYGEGNWSKIL LHYKFNNRTSVMLKDRWRTM KKLKLISSDSED
4126	34494	A	4167	1	1345	IPGSTISCLKGQYPSEPFNMAED VSSAAPSPRGCADGRDADPTEE QMAETERNDEEQFERQELLEC QVQVGAPEEEEEEEEDAGLV AEAEAVAAGWMLDFLCLSLCR AFRDGRSEDFRRTRNSAEAIIHG LSSLTACQLRTIYICQFLTRIAA GKTLDAQFENDERITPLESALMI WGSIEKEHDKLHEEIQNLIKIQA IAVCMENGNFKEAEEVFERIFG DPNSHMPFKSKLLMIISQKDTF HSFFQHFS\YNHMMEKIKSYVN YVLSEKSSTFLMKAAAKVVES KRTRTITSQDKPSGNDVEMETE ANLDTRKRSHKNLFLSKLQHG TQQQDLNKKERRVGTLQSTKK KKESRRATESRIPVSKSQPVTPE KHRARKRQAWLWEEDKNLRS GVRKYGEGNWSKILLHYKF\NN R\TSVM\LKARWRTMKKLKLIS SDSEDWIVFVKL
4127	34495	A	4168	3	378	LTSGSRADQGEGQEEGAEGGR ASSSSSSSPRGPQHHPHLHGDP AEHRPGHPLCSPPDLTVAYQ/M PEVPAEDM/SDPSFCSARQGGQ RGLDSGPGAPWSSSHSPHSRFQ EASHGACAGWRWCRQEEL

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4128	34496	A	4169	1	1044	SGQEVNKEDGQADVQQDHHADEDGVGDLARQPHLFHLHLRLCRQCGLLPRLLLGPRLGQPSSLSLAGLGPGLGFGDDGLGLQLGGGLACRLGASERGGLQRGGGRGRGRGLGPG/GPRARAGPQRVGARAAWCAQHSCGSPGKAPPPAPA/TGAGGACRASMAMRSVAGRAGLRRPAPSDGVTDRLPSPLGSPFQAP/EAQQAVLGHPGPGPLGLRGRPGR*RGATLGPRGLT/PRAAAGSRGAAVGGPLRRRPGRGAPAGSPSSPGSPAAAGASDIPDLAGRSPEPAPWPKCEQCWTPGWQPGRPVPLPQLWPWRGLSISGSMPLGEGLEDGSDPMTPSCCLPGT
4129	34497	A	4170	1	732	SLTQAGTVSLGLDAEGQEVFVPFSAVLPMVAPNDLVFDGWDISSLNLAEAMRRAKVLDWGLQEQLWPHMEALRPRPSVYIPEFIAANQSARADNLIPGSRAQQLEQIRRDIRDFRSSAGLDKVIVLWTANTERFCEVIPGLNDTAENLLRTIELGLEVSPSTLF\AVASILGGLCLSFNGSPQNTLVPGALELAWQHRVFVGGDDFKSGQTKVKSVLVDFLIGFRLQRP/VSIVSYNHLGNN
4130	34498	A	4171	1	908	MEKAPPQTQHEGLKSKEHLPEQTDEGKTEYRRVPSLRAVVLFRQRSCIENILRACVGLPPQNHMLLEHKMERPGPSLKRVGPVAATYPMLNKKGPLVWEVSPATLFAVASILEGCAFLNGSPQNTLVPGALELAWQHRVFVGGDDFKSGQTKVKSVLVDFLIGSGLKTMSIVSYNHLG\NNDGENLSAPLQFRSKEV\SRSNVVDDMVA\SNP\MLYTPGEEPDHCRMGRNLPE*GSS
4131	34499	A	4172	85	529	ECGARPGSSTRPPARLSPRLFCSAIRAALKTRPAPALACTWRTG*RASLPTTRCAGSGLGTCTAEGSEGCSHPGPLTGTG/RQEACPGTAPAGSPSCLHPRGRPRPCPPGTLAPRMSCPWPRSPPLTRYLPSGENLQSKLESLNTSEKF
4132	34500	C	4173	215	324	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
4133	34501	A	4174	2	505	YKCEVCDKVFNQN*FLVCHNRCHTGKKPYSCYECGKTFSQTSSFTCYRRLHTGGKPYKCSEHNKTFG*NSALVIHKAIHTGENPCKCNECGKVFNQKAHLARHHRLHTREKPYKCEECEKVFSRKSHLER/HKLKRGGVALV/C*ECPTVYQNTSCLRSLSCSYPMSLNG
4134	34502	A	4175	1	6192	
4135	34503	A	4176	2	3389	
4136	34504	A	4177	3	875	GEEAALSLCMHSTDDATRLGARDTEPLWHVPAQ/ARLSAIAGSSGNKHPSR/QDAAGKDSPNRHSK\GSKPSAGSLRLSSREGEDRTAWTGPRGAVEQEVTGPDLC*GRGQQGLLVGWT**EQKRGQGKPQYSSHSSSNTLSSN/ASSSHSDDRWFDPLDPL/EPEQDPLS/KGCMSLAK/APRPAKPHKPPGSMGLC/GGGREAAGRSHHADRR/REVSPAPAVAGQSKGYR/PKLYSSGSSTPTGLAGG/SRDPPRQPSTLWHRTWYL/YHTASAAVHRGLCRELEQADQIPPSWYGRRPMGNS
4137	34505	B	4178	108	318	
4138	34506	A	4179	103	540	RRGCESHKTLRRGTSWGLDARGGGPGPGQVSAGRDGAEVWLSTCDRGHALSGSVEELLFLQN/GARTER*EGPGEWPRPPPPGLASPALWRFWAEQVGGSFQELESPSCRTARGSSRTWGSILQNSSWLFQDLGLHLAEGCFLETP
4139	34507	A	4180	33	896	KITRHCTAPGKIRIVPKESQESTPQQDGAPGPGRATSCSARWSPRSWKSHELFCKMEPQVLEEPRAVLQDGAPGPGRATSCSARKGRGPEKPVQGLPN/GSVRAHSGGRAAPQPSPRGHGPGRG*TAAPLPHLCPLTPVLLQG*GPD*WPLGWATMRPLPLRAQPAPPPPHWMLLTPSAPPPGTGKPQGGRGQTSGSCVPATDPHCRLSAPSPGKLGPPCDFLEPP*QRTTNWGSSEAGSPKSRCPRGHVPSGGSKGGIFLSLHFPGAPQSLEFPGSQPHGLIGAS
4140	34508	B	4181	1	625	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
4141	34509	A	4182	160	1149	FASERMKVEPWRAGPGRRAWSEGAGQAPQKRARAGAEPQLPATPALPGGKMVARRTKLA\RGTRRT\YPEPTV\YAAIPIKFSEKQQASHYLYVRAHGVRQGTKSTWPQKRTLFVLNVPPYCTEESLSRLLSTCGLVQSVELQEKPDLAESPKESRSKFFHPKPVPGFQVAYVVFQKPSGVSAALALKGPLLVSTESHPVKSGIHKWISDYADSVPDPEALRVEVDTFMEAYDQKIAEEEAKAKEEEGVPDEEGWVKVTRRGRR\LCSPGLRQPACGCWRGRDGSAA\KRAAQLLRLAASREQDGASSAA\RKKFEEDKQRIELLRAQRKFRPY
4142	34510	A	4183	2	361	GTMVARRTKLA\RGTRRTGIPSPPC*A\AIPIMCSEKQQASHYLYGRAHGIQQGTKSTWPHKRTIFAFNGPPYCSEQESLSCLQSTCGLVQSVKLKEKLELGWESRSKFFHPKPVPVTEEQ
4143	34511	A	4184	917	1128	
4144	34512	A	4185	1	660	MAWQMMQLLLLALVTAAGSAQPRSARARTDLLNVCMNAKYHKTQPSPEDELYGQ/C/SWRKNA/CSFTSTTQEAHKN/TSHLYGFNWNHCGEMVPACKRHFIQDTCLYE*PPNLGPWI\RRYAWLPGIQELAEELNFPGVSAGSNPSSSSIQGWVPGILEPEPFFSTKISQVDQSWRKEWVLNVPLCKEDCEQWWEDCRTSYTCKSNGHKGWNWTSGSNKCQVAAA
4145	34513	A	4186	216	781	MDMAWQMMQLLLLALVTAAGSAQPR\SARA\RTDLLNVCMNAKHHKTQPSPEDEAVWPDP/WMCKGSCRKTKSWNI/HRKSKCEVGLA/WEACSVSAGTGRGPGCGRWVGAPQGP/CPRKCSSG*PTW/VQRSQNMEEMAVVNQSWRKERILNVPLCKEDCERWWEDCRTSYTCKSNWHKGWNWTSAPSAVCDPLL

SEQ ID NO:	SEQ ID NO: of peptide sequence	Met hod	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
4146	34514	A	4187	3	625	QCRPWRKNACCSTNTSQEAHKDVSYLYRFNWNHCG\KMAPDCKRHFHPGTPALYE/CAPHNLGAWDPAGWIQSWRKERVLNVPLCKEDCEQWWEDCRTSYTCKSNWHKGWNWTSGFNK\CAVGAACPTF\HFYFPTPTVLCNEIWTHSYKVSNYSRGSGRCIQMWFDASPGATPIEEV\ARFY\VAAMSGAGPWAAWPFLLSLALMLLWLLS
4147	34515	A	4188	1	268	EQGRH/GSSTPVGPRGGPR\GAEHAPKHQGCGDRAGPQVGMDQRRRDPPRAPAAPRPWCGQRAALSSLGGSHLCDDA*VQPSAGLGKVLKF
4148	34516	A	4189	2	1632	WKRCPGLPRAAATFPSGSGAGGARREAGGRAPTPGPASPRTARGHARNSPAPARTAGRTGSAGAWQTPCPAPLFPMSAGLPAACHWNPV*LRALKTG/LEGVLGGSADTQHNRVTDGSLAPN\AACVYTPKINGNRHPNTCTKMFIVSLDAKGKKWKQPTVHQQRKRETCGLHPRKCLQYTPS*WSTTTGILPSRTPRISCVQFVKKKLGQAGLLGHPGACLLCTLP*\PAGVGTFLFPRGC*GVVH*LETHTCG
4149	34517	A	4190	2	87	
4150	34518	A	4191	3	291	
4151	34519	A	4192	112	286	AWLLWLTSLPWGSLYALALLANKPAL*SLLLLRYTLLPPHHQCEKVPRWNEPQPTLFP
4152	34520	A	4193	1	933	
4153	34521	B	4194	1	999	
4154	34522	A	4195	135	1160	VWALVRSTLELFHTDDEEEGEYDEVTEEVTEQVYLPAKAKVAQEEEVHPYPSAPPHYYFEEKEWPDPPDLSFLEDTGRKVVAPVTEQHLERLLSVLFRQEFSRLDERDDAVEQLRGVCIRAWEKITSGGEQYPSFSAVKQGPKELYADFIAWNLLRQESLKKVISDSAAQDIVLQLLAFGNVNLDCQAALRPIRGKAHLVDYIKACDGIGAKQDSERFAFTIPVVNNLQPAKHFHYFTDGSSNGKASYSGSKGQNQQPIWILSRHLKPYHEPDAKEEIPGG/CPRTPWLQPCRD*C*GGP*/PVTSNTR*TQPPTWGQIKKLSQMVEENLRKAGQLVTMTVYWN

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4155	34523	A	4196	502	578	LV*EDCIAERAEVLRNESYGIIDWSP*GMFSLNCTSQSACHGHTMFSW
4156	34524	A	4197	2	408	
4157	34525	A	4198	3	853	LLKVIMSAKIFTKKNENSTERLCGDGEKRGPDFRTERSVWLLRLEEAVAMVQRGSRAPESRVVAQVLTLLDGASGDREVVVVGATNRPDALDPALRRPGRFDREVVIGTPTLKQRKEILQVITSKMPISSHVDLGLLAEMTVGYVGADLTALCREAAMHALLHSEKNQDNPVIDEIDFLEAFKNIQPS/LVFEASLGLMGIKPVDWEEIGGLEDVKPEVKTAH/WSLRQKSGHC/RSCARLPTGLLATLGSGSGSGRATEAVSGPAG*KRASIGGSSQRPRRFPT
4158	34526	A	4199	266	370	AERINSITVFSETLKRFLQASGK*FHRDIHNSRN
4159	34527	A	4200	1	1780	MGDVNQSVASDFILVGLFSHSGSRQLLFSLVAVMFVIGLLGNTVLLFLIRVDSRLHTPMYFLLSQLSLFDIGCPMVTIPKMASDFLRGEGATSYGGGAAQIFFLTLMGVAEGVLLVLMSYDRYVAVCQPLQYPVLMRRQVCLLMMGSSWVVGVLNASIQTSITLHFPYCASRIVDHFFCEVPALLKLSCADTCAYEMALSTSGVLILMLPLSLIATSYGHVLQAVLSMRSEEARHKAVTTCSSHITVVGLFYGAAVFMYMVPCAYHSPQQDNVVSLFYSLVTPTLNPLIYSLRNPEERSHRGVKLNECNQCFKVFSTKSNLTQHKRIHTGEKPYDCSQCGKSFSSRSYLTIHKRIHNGEKPYECNHCGKAFSDPSSLRLHLRIHTGEKPYECNQCFHVFRTSCNLKSHKRIHTGENHHECNQCGKAFSTRSSLTGHNSIHTGEKPYECHDCGKTFRKSSYLTQHVRTHTGEKPYECNECGKSFSSSFSLTVHKRIHTGEKPYECSDCGKAFNNLSAVKKHLRTHTGEKPYECNHCGKSFTSNSYLSVHKRIHNRWI*/YYCRNFWRKALIDLSSLR*FERAHTGYISYLLQH
4160	34528	C	4201	18	182	
4161	34529	A	4202	1	389	
4162	34530	C	4203	114	548	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
4163	34531	A	4204	122	735	LRAQQQHN*VLTLHKPACTLSTTS*K*LHKIRK*LWHLRDRAPFIFTSEMEYFITEGGK/NPQHFQDFVELCCRAYNIIRKHSQLLLNLLEMNSYNGYVGLLHNILQLEREGLATKEELQQNFPPLSVSLPFDQSINQISEHRSLIFNGQYPYGSCWFRQAVCKLIQKYAGEWGWIATAELRAEIDLNVLKFTIQVLSWKVQASLQ
4164	34532	A	4205	139	4496	KMAYSWQTDPNPNESHEKQYEHQEFLFVNQPHSSSQVSLGFDQIVDEISGKIPHYESEIDENTFFVPTAPKWDSTGHSLNEAHQISLNEFTSKSRELSWHQVSKAPAIGFSPSVLPKPQNTNKECSWGSPIGKHHGADDSRFSILAPSFTSLDKINLEKELENENHNYHIGFESSIPPTNSSFSSDFMPKEENKRSGHVNIVEPSLMLLKGSLQPGMWESTWQKNIESIGCSIQLVEVPQSSNTSLASFCNKVKK
4165	34533	A	4206	1	3150	MEKPRPLEAPSAWPQDDVQCGVTVGMDGAAVRANRTPWPQDLEQTKWIEIKKSAFTWSSQLSLNRGFLTCKDENNNAGLLRVSSYSSREDQLKNIASDSLFMLPGGLCQSPTGTSHCSNQMETQGQGSPGGAVRGDKALGPEKARQGCGMNGSGKYCKFRVLAIQGKPECLATLMQPDLGDSPGLREMNVVEHLRASFPVEQWYWRGGQRGEAEGARSSKAENNTSLICNFRLDYAPIEKQWDLHFADYFAEDLK
4166	34534	A	4207	1	1203	

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4167	34535	A	4208	1	1470	MLHSRGFLAEVFGILARHNISV DLITTSEVSVALTLDTTGSTSTG DTLLTQSLLMELSALCRVEVEE GLALVALIGNDLSKACGVGKE VFGVLEPFNIRMICYGASSHNL CFLVPGEDAEQDGTGTSGIGAQ KKKMYANNGAIDRKLLFEATF VTIEKCCDTNQKGDDTHALGQ PIRGHDKSLAGSFCYACRSEEG LSQYRAYDSRGQLIAVKDTQG HETRYEYNIAGDLTAVIAPDGS RNGTQYDAWGKAVRTTQGG\L TRSV\EYD\AAGRVIRLTSENGS HTTFRYDVLDRLIQETGFDGRT QRYHHDLTGKLIRSEDEGLVTH WHYDEADRLTHRTVKGETAER WQYDERGWLTDISHISEGHRV AVHYRYDEKGRLTGERQTVHH PQTEALLWQHETRHAYNAQGL ANRCIPDSLPAVEWLTYGSGYL AGMKLGDTPLVEYTRDRLHRE TLRSFGRYELTTAYTPAGQLQS QHLNSLLTYRHANFAL
4168	34536	A	4209	757	907	RRYCRITVRWQSM/WADNRIA VDAHYPYR*CRS\GRVTEKND\ LIPKG\VIRTDDERTHRYHYDSQ HRLVHYTRTQYAEPLVESRYL YDPLGRRVAKRVWRRERDLTG WMSLSRKPQVTWYGWDGDRL TTIQNDRTRIQTIYQPGSFTPLIR VETATAVMDRILKDHQIVVDIP HGEAWLRDDEERPMILIAGGTG FSYARSILLTALARNPNRDITIY WGGREEQHLYDLCELEALSLK HPGLQVVPVVEQPEAGWRGRT GTVLTAVLQDHGTLAEHDIYIA GRFEMAKIARDLFCSERNARED RLFGDAFAFI
4169	34537	B	4210	1	3258	

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4170	34538	A	4211	281	1571	CQCPGAACPTTSCRVIPHWA\YDEADRLT/HRTVN\GETAERWQYDER/GWLTDISHISEGHRVA/VHYRYDEKGRLTGERQT/VHHPQTEALLWQHETRH/AYNAQGLANRCIPDSL/PAVEWLTYGSGYLAGMK/LGDT/PAANLDIRIPYATDPA/GNRLPDPELHPDSTLSM/WADNRIARDAHYLYRY/DRHGRLTEKTDLIPEGV/IRTDDERTHRYHYDSQ/HRLVHYTRTQYAEPLVE/SRYLYDPLGRRVAKRK/DRTRIQTMYQPGSFTPL/IRVETATGEQAKTQR/RQLADTLQQSDGEDGGS\VVFP\PVL\VQML\DR\LESESSADRVRSFISLANQSKCVEHAY*RWQCHLGVCWWSSHQIPAVPLTGSVTRWHCHLASSSEAGSVAWLPHLSEGHSNRTSSPELLRSRMCAWHTLSAQSVHLVSLYILEILALMNSINSL
4171	34539	A	4212	311	788	
4172	34540	A	4213	29	395	RIFHSVI\GVAAHKGGVYKTSVSVHL\AQDVAEIT/LLEGNDPQGTVS*YQGPGRTLIPLEAALRNIAHSLSIPPPKIFAAPTLRHYFALFFCGHSLFAPHIELLEAGTVLQLPQGPWSSPTSF
4173	34541	A	4214	1	1033	MKMPEAIATKEKIDKWDLIKIKSFFSTPKETINRVNRHHTEWEDISAIHLSDKGPISYIYKNLTRFTRKKQPHYKVGKGNEQTRILESHPHLLKGLASTPFDSEGVRTERRDIIKDGILTQWLLTSYSARKLGLKSTGHAGGIHNWRIAGQGLSFEQMLKEMGTGLVVPGTAENARSCIRAYFYDIHETLCRQEEMALSVVDDHVREKLIWLRQHQEDMTILLSEVSAACLHCEKTLQQDDCRVVLAKQEITRLLETLQKQQQQFTEVADHIQLDASIPVTFTKDNRVHIG\PKM\EIRVVTLGIGMGAGKNLLSLF*V*NRVEFHGSPFPTIWFLTWETVGFLK
4174	34542	B	4215	414	1022	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
4175	34543	A	4216	896	1626	NATTIRYEHQRVLKAAQYLHQQGITRCNSSSTLTSAAPGRVDSPPTSMIVAPALIIRFACFTASISELCVPPSEKESGVTLRIPITHLMRELTCRLIRDKSATVTGSHTLVVARHCCYAAPGGCCLLANWLKPGLFGPIGVLSRRGTSVILPIGGFYQWNPMICPNGVVPMQHG*RRGLAQERPLEEWLPVCRDMLNAFFLPDAETEAAMTLIEQQWQAIIAEGLGAQYGDAVPLSLLRDELAQRLDQERISQRFLAGPVNICTLMPMRSIPFKVVCLLGMNDGVYPRQLAPLGFDLMSQKPKRGDRSRRDDDRYLFLEALISAQQKLYISYIGRSIQDNSERFPSVLVQELIDYIGQSHYLPGDEALNCDESEARVKAHLTCLHTRMPFDPQNYQPGERQSYAREWLPAASQAGKAHSEFVQPLPFTLPETVPLKRYNDSVRAPTCAESRAIFTSTRNNTLQLFFNANFRRPWARGLATNVNDRRASVDHQIRMFHRIYQRVMRATIRKGIRRDVEDPHYSSDAGTYLSPNSRQISNGNWQSHIGRSPSLLLCRTWGLLFTGKLVETRFIWPNRGVIPTGNERYIAHRRFLPMEPDDMPQWRCPHATWLAEAKMFDSLAKAGKYLGQAAKLMIGMPDYDNYVEHMRVNHPDQTPMTYEEFFRERQDARYGGKGG
4176	34544	A	4217	838	1575	CFFLSPSPPSSPPSPNRSQTTEEETKRQE/ERERKREEEEEKKGRRKETKKRRNRQEGKQHRKEEKEGEKQTKQRTETERETKRRRENEQAKAHKGTRKRKEEQKKAKAARRRTHKRQNPSRGREGTHPKQRQGKEE/VNRQNKEEAKQKREEAGRTRR/EDRGRKDDKKERRQQQTEKKAKPKAEHGQERTDTTTKKARQREGRPSERRRREREE/MSKHDPQNRAEKTNEEKEEGRQHER*TQKSSTGI

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4177	34545	A	4218	1	692	MNALHAEALEMTSQFDQELAAKFEADHEMALLMNKDFDRDREEQRRLAEQARREHEERIKREAAEQARRDAEAKHKAEIEAAARREAEEKARAELAERQRIEAEQRAEREKKETEERARREKEEAVAAERRRQEEAEAARLVEEQRKAEEEARRAADKEHRRTVNRR/GLRRSDCSGHPRRIRTESSAGDRWRQSAGRAHQILRQT*THTSLTTASKNGAGLSSNSPTRKRS
4178	34546	A	4219	3	1120	
4179	34547	A	4220	1	831	MVKARKIMETPQPAWEMRVRICTVDWSKLNPYIPDDFSLIKSEKKYDHPELIVDESNLRVVYAPSRYFASEPKADVSLILRNPKAMDSARNQALLEGYFSFTATEDQLEQAKSWYNQMMD/SPEKGK/.FEHGNMPA\QMLLQVPYFLRE\EREH*IIITPILHMRKQEQSG*/RNLPKAAQLSMMQDLQTLLMAASYCSELGHVATQFQGMLACTRNPNSWDRNSETSGKAEGFIPMQLGDVADPSVRCSSVSSLWGHSSPKLLRSVCMANRICVKLQRWT
4180	34548	A	4221	1	1503	
4181	34549	A	4222	1	1113	
4182	34550	B	4223	1	760	
4183	34551	B	4224	1	1755	
4184	34552	C	4225	1	4215	
4185	34553	A	4226	1	3240	
4186	34554	A	4227	1989	2144	
4187	34555	A	4228	1	1203	
4188	34556	A	4229	1	4767	
4189	34557	A	4230	31	512	EYRKSPDIRPIVIQHGEEAEITHHFR*QELADKTLIFEITHREMQRFQPVGTGDIREPVFVFFRWRLTNPFNILEHGEPEGIRVDAAVPRAVIGGLEDHIGVAVQKLQHKTFRYFPFIIQMVKDGVVPEGRPAFVHHLSLFLRIKILAHLTHNTQDF
4190	34558	A	4231	369	918	RPGMSNPWRDLFRTGVDPTNDRLSALVEI/YRMMRPGEPPTREAAE/SLFENLFFSEDRYDLSA/VGRMKFNRSLLREEIE/GSGILSKDDIIDVMKKL/IDIRNG/KGEVDDIDHLG/NRRIRSVGEMAENQFRV/GLVRCTGTVPPFLHQQKCEYHL/PQRPVASTLSRYF*HFRLRNFSMPRANEIKKGMV

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4191	34559	A	4232	3	1012	SVVLKIVERVDGYFPSPPLFLGAAFGSHVRSRALPDPCVLFRVTIYLCVLASVARTFSPLLPVSRKKHITPLGGFQLHETHLCLQDCRTIILRPRLGEFGNKFSQLVDTIDLH\NQHGLAHL*KESARGQYSLLLLGMVSLCALILILWRVVYRSVTCPLADQTQALHRLLDGDIVSPFPETAGVRELDTIGRLMDAFRSNVHALNRHREQLAAQVKARTAELQELVIEHRQARAEAEKASQAKSAFLAAMSHEIRTPLYGILGTAQLLADNPALNAQRDDLRAITDSGESLLTILNDILDYSAIEAGG\KNVSVQSYVARLEPVAASGWHKYPWLN
4192	34560	A	4233	1	502	
4193	34561	A	4234	1	653	
4194	34562	A	4235	2	300	YALATPPLSV/INQWQLALDKGQLPTF/VAGLAPQHPQYAAMHESYWPYSALR/EILQRTGMLDGGPKITL/PGDDTPTDAVVSPSAVTNSHGR*VPTLGGVWGL
4195	34563	C	4236	40	105	
4196	34564	A	4237	355	526	
4197	34565	A	4238	116	949	RPGTGRCSAVQLPVLLLRGPHSSHTVGTH\MVDLDSGQLCVYPGNSDESMPAATQARERLLADTAKKKAQIAELQSFVSRFSANA*KSRQATSRARQIDKIKLEEVKASSRQNPFIRFEQDKKLFRNALEVEGLTKGFDNGPLFKTLNLVL\EVGENLPVLGTNGVGKSTL\LKTLVGDLHPDSGTVKWSENARIGYYAQDHEYEFENDLPVFEWMSQWKQEGDDEQAVRSILGRLLFSQGDIKKPAKVLSGGEKGRMLFGKLMMQKPNILIMDEPPTHP
4198	34566	A	4239	1	319	MVKKMARAPMI\L\ALANPEPEILACRHGRKEVRPDAIIC\TPGRSDYPNQSETNVL\CFPANVHRIPQAASHLRAHQSRIPISLMSISAKILTYLLANQIQFLVKQH
4199	34567	B	4240	263	1390	
4200	34568	A	4241	1	323	
4201	34569	A	4242	3	1855	

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4202	34570	A	4243	2	964	LLKHGVSLYIQDKEGLSALDLVMKDRPTHVVFKNTDPTDVYTWGDNTNFTLGHGSQNSKHHPELVDLFSRSGIYIKQVVLCKFHSVFLSQKGQVYTWGHGPG\GRLGTWEMNRHAWVPRLVGRD*MVIIVSPSWPAAKDHTVVLTEDGCVYTFGLNIFHQLGIIPPPSSCNVPRQGLHNRQNRRYPPVPGSAGPTSMEPSKIRPTGLKFSLTTQQQSEIDLGCSSLCWDYRREPLRLAYWFIKKDIAKDTDEETRRHGVSLYIQDKEGLSALDLVMKDRPTHVVFKNTGSLQFQSIPSCRESQILSEKQGDLFREEPMFGS
4203	34571	A	4244	1	725	FRVDPRVRKHFGLFYAMGIVLMMEGVLSAC*HVCPNYSNFQFDTSFMYMIAGLCMLKLYQTRHPDINASAYSAYASFAVVIMVTVLGVVFGKNDVWFWVIFSAIHVLASLALSTQIYYMGRFKIDLGIFRRAAMVFYTDCIQQCSRPLYMDRMVLLVVGNLVNWSFALFGLIYRPRDFASYMLGIFICNLLLYLAFYIIMKLRSS*KVLPVPLFCIVATAGMWAC\ALYFFFQNLSSW
4204	34572	A	4245	1	833	MKPVWVATLLWMLLLVPRLGAARKGSPEEASFYYGTFPLGFSWGVGSSAYQTEGAWDQDGKGPSIWDVFTHSGKGKVLGNETADVACDGYYKVQEDIILLRELHVNHYRFSLSWPRLLPTGIRAEQVNKKGIEFYSDLIDALLSSNITPIVTLHHWDLPQLLQVKYGGWQNVSMANYFRDYANLCFEAFGDRVKHWITFSDPRAMAEKGYETGHHAPGLKLRGTGLYKAAHHI/KAHTL*VCFHAADKGIPETEKKRRLNWTYSSTWLGRFHNHGRG
4205	34573	A	4246	1	672	GTQNAVNG/VIIFLSWGDAVKSFWIYRGGRKREGPLFHA*Q\FLIYTIIIRAVGSIINYVIANYKLKFITPGVIDFICTSLIAGILTIKLFLLINQFEKQQIKKGRDITSARIMSRIIKITIIVGLVLLYGEHFGMSLSGLLTFGGIGGLAVGMAGKDILSNFFSGIMLYFDRPFSIGDWIRSPDRNIEGTVAEIGWRITKITTFDNRPLYVPNSLFSSISVENPG

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4206	34574	A	4247	1	347	PLRP\GQPGPGGAGT/RALRAPPLPSSSELCYGPGQPGRWPRCPQFPSLPPHSS*LLHTGHWPCTLGYCFIPILRAAPPLPCKCASPVL\SCTYPLPAAPSLPVLVHTSIKCFCFHLQ
4207	34575	A	4248	43	446	VLPAVPRPGQ/PPCVPAPVQAPEPPRPSPGWSQATGSPGPAGAAPSWR\GLPAVPGHTAGVLGPGPPGQRQPGPGGAGTQLCGPHLFLRLLNVAYGPGQPAL/RNVPLQTAPALTPSPQHLLCPFLSTHLLNASVFIC
4208	34576	A	4249	1	1521	RIPESRLPTTAFVQAPWARSGSSGLRRWEKHAGQQVGWWARGPGVRGRQAAGGGAAALTCRGGAGSAVRSCAGLPSLASGSAGCRLHPSYSFGFKVGS/PTVPAALSS*STS/RGREHGGVTVVPVMTQNPRS\PDGPARVEDCEAIA*GTGWL\QQGIGTRPPGTGLGRAR\GAPAVPQWNPV\KSCQGPGHPNRLPSHGPSSGEAGRGW/RGLQITPQL/PEVTHRRVLPGDHPATEA\GGFGTG*PGLPGRVPGPGVGGTYQAKALTPLGPVGLLAPASCAQCLQQSADGPGATGHL*ELAESQCRRQPTG\PPGQLAVSGWATVPGVPAAPRPFGPAQQPA/SVPTPSYWA/GSPGAAAWPESHRR*ACDWAW**VLPAVPRPGQ/PPCVPAPVQ\PQSHRGPAHDGARLY*GLPQAEQLHPGGGLPAVPGHTAGVLGPGPPGQRQPGPGGAGTQLCGPHLFLCFLNVAYGPGQPGRWPRCPQFPFLPPILSWNIFGVGTQKKKKKNQSFLKKKKKK
4209	34577	A	4250	167	582	RSLGLAVTEMVPWVRTMGQKLKQRLRLDVGREICRQYPLFCFLLLCLSAASLLLNR*RRSAEPGRRL/SL/LKVQTPGPCCLTVRRPRSCGTGDQWGERAPQRSGLGEHGGASRPEAQAGGVGLIASFPEASSPELPFSHP

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4210	34578	A	4251	402	1465	DLILSHPTAWFTIKYKPKQLGLQELFPQGHSCAVCGKVKCKRHRPSLLLENYQPWLDLKISSKVE\ESLSKDLELVLENFVYPWYRDVTDDESFVDELRITLRFFASVLIRRIHKVDIPSIYNQETIKSSNESI*KWIVKARQKVKNTEFLQQAALEEYGPELHVALRSRRDELHYLRKLTELLFPYILPPKATDCRSLTLLIREILSGSVFLPSLDFLADPDTVNHLLIIFIDDSPAEKATEPASTLVPFLQKFAEPRNKKPSVLKLELKQIREQQDLLFRFMNFLKQEGAVHVL\QFCLTVEEFNDRILRPELSNG*NAVSS/WKNCRRFIKHTVWMKVLTKLDLIPSLVEEIPR
4211	34579	A	4252	1	1232	FPGRRFRLVVRLRGAEAASERQVYSVTMKLLLLHPAFQSCLLLTLLGLWRTTPEAHASSPGAPAISAASFL*DLIHRYGEGDSLTLQQLKALLNHLDVGVGRGNVSQHVQGHRNPTTCFSSGDLFTAHNF\SEQLRIGSSELHEFCPTILQQLDSRACTSENQENEENEQTEEGRPSAVEVWGFGFLSVSLINLASLLGVLVLPCTEKAFFSRVLTYFIALSIGTLLSNALFQLIPERSYKNKAQVDSLPTFLAQAGMLLWRVRIRRRVVDPIRESWMLPFTKIPLWGYGLLCVTVISLCSLLGASVVPFMKKTFYKRLLLYFIALAIGTLYSNALFQLIPENRRKWWQPVHNTFGGSTAWHTDKSIEQSIDTLFDEVKKESEKETPSLQIGDLGPQESLKTFNNTNSPHH
4212	34580	A	4253	3	924	VGACTAAARPLPIPQLQPILHHRGEKSQLWAHSGSSWGFLAVAAVPPSHLCPPLQSRGWKRPP/PLASAGVLPGCCCCACLVSPSLAQPAG\LGPKPAAPLGPGPWVSVAPCSRPGPCPGTRSPA/P*GHPAMGR\GVHEPRVGPAPPEKAIITETGAGLAERRGQGLGGGSSFRSAEPQGCRSLGPQSPGGDPAHTILRPPSQNGDCAEMHACRLHPAILGTHGTGGLAAQSHAPRALLPSCPSSQQPADGWCSLHLCLPGLLLAPRIHGPSTREGGPGHGTPGPTNPASSGATRGTRRVRPSVPRSPTL

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4213	34581	A	4254	1	318	VADPVGAARAGGQPLAGRVW PRAGGGHSPRVLGAAGPGPHV CTLRLPGTAIRTEPGAPLACAR AWPGSSPAG/PECLPTSC*P*EG QEPSSHVASLPWGPGVGETQ
4214	34582	A	4255	1	718	FFFFFFSFLCHLYWVSPTPGPHG KLANMANWAPWPS*GLSKLVG KHSCPAG*LPGHARAQASGAP G/ISPDSSAREA*ECT/PCGPGPA APSTRGECPPPSSRPHS/SQQDP GRCSFAPAVPQDAGGQGHWCC APATGHSAPRGCPPARAAPTGS ATPAPPPAACAASSLSMVSAPS R*TTGIASSGTSIPETKHQGTPG TAPAGT/GPGGSTGPKA/PGPAP AHPTRLAGTSGHTAPPTCPPAV
4215	34583	A	4256	702	1026	RSGRTQRAAGVSGSALHQVQS WP\HLKISADQRAGLLF*EHPFP PSASSGCLDVSISSYPVGSD*FIN GMARANGRWKTFTGLHSGKPL GFSDAFCQHHNLIILCWKTW
4216	34584	A	4257	170	1049	RGSGCSAELVPSSRWRPGSRAG AAAGTETPG*PRVYVPAGNGE AGGPGAAWARRAAALPGTAA GPPRPAARPGAAPARGGPAPGA PAQALPR/TPTWPAAR*AQRAP SPPSWGS\AQPGHPGDLAAGVG RGAGGGHSRRGRHHHVRSLAD LLQLPGAAEGAGDRGHLPGPD/ GERS*AASSFSAAGRAAGTASC CSAGGTPPSPCTILSTSSSSLAH VASSS/RRRAEGDTKVS/RGRAE GQDSETGREPGVLHRGSGRTQ RAAGVSGS/RSAPSPVVATTSRS LLTSVQGCFSENILSP
4217	34585	A	4258	178	556	QSPQEHFHPECGRRDILCQVRQ EIRWPNPGEVHHLGLEICPVWI LQLHLALRTRAPEHPLQVHRPG GGAV*RGVPPPLRLLQACDGPE VPAAGRPRPARSSPGQWPP*/PA AVAPPVTERPPTPSAA

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4218	34586	A	4259	5	1044	TGRILDGWHWAKELRLDCPLG DSRRPPFSRVSTEGSPAFLALRL PNVTAGS*EVSMLASTETPLVIT RPSPG\GHDPGPAPRGAAASPA GSPAP*QKSPRPLSAAAPPLLAS DPAPPRAAAPPADTESSVQPPA APHAGPWT\PSAPGPLDVHSPPP \PSRGPFVQSSAEPHNRPSPGAT RPRP\PPRGAAASPAGSPAP*QK SPRPLSAAAPPLLASDPAPPRAA APPADTESSVQPPAAPHAGPWT LERSWAP*RSLPTPIPVADPLCR APLSHRYP*GDCQRSGLCHTSP GRASHLPGPGAHKRTPHACWL PLECHRRSPHP*THPSG*PGPSP QSFFPEFLGSGP
4219	34587	A	4260	2	576	CLVNSTTRRSFQLRLVPVPKFQ PPHMTVR*LFNFGRQLTATTFS/ LRKSYAVREAYELQNCPDPPPF QNGYMINSDYSVGQSVSFECYP GYILIGHPVLTCQHGINRNWNY PFPRCDAPCGYNVTSQNGTIYS PGFPDEYPILKDCIWLITVPPGH GVYINFTLLHTEAVNDHIAVW YENLSSQNICDCDQQF
4220	34588	A	4261	1	837	MWAGNAWRAALSGVPCGRSA QSVLAQLRGILEGELEGIRGAG TWKSERVITSRQGPHIHVDGVS GGILNLTSVRFIRGTQSIHKNLE AKIARFHQREDAILYPSCCDAN AGLFEVLLRPEDAVLSDELNCA SIIHGICLCKAHKYHYCHLDVA YLETKLQEAQKHRLFLVATDG AFSMDGDIVPLQKICRLASRYG ALVFVDECHATGFLGLTGQGT DELLGVMGQVTIINSTLGKALG GASGGYTTGPGPLVSLL/RAQP YLFSNSLPPAVVGCTSKAL

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4221	34589	A	4262	1	2142	MIILIDAEKAFDKIQQPFMLKTL NKLGIDGTYLKITRAIYDKPTA NIILNGQKLEAFPLKTGTRQGCP LSPLLFNIVLEVLAQAIRQEKEI KGIQLGKEEVKLSLFADDMILY LENPIVSAQKLLKLISNVSKVSG YKINVQKSQAFLYTNNRQTESQ IMSEFPFTIATKRIKYLGIQLTRD VKDLFKKYKPLLNKIKEDTNK WKNIACSWIGRINIMKMAFPR WELNNENTWTQEGEHHTLGPV VGWGKRGGIALVDIPNVNDKL MVLEVLARAIRQKKEIKGIQLG KEEVKLSLFADDMIVYLENSIV SAQNLKLISNFSKVSGYKINVQ KSQAFLYTNNRQTESQIMSEFP FTIATKRIKYLGIQLTRDVKDLF KENYKPLLKEIREDTNKWKNIP CSRIGRINIMKMAILPKVIYRFN DIPIKLPMTFFTELEKTTLKFIW NQKRACIAKTILSKKNIAGGITL PDFKLYYKATVTKTAWYWYQ NRDIDQWNRTEASEVTSHIYNH LIFYKPDKNKKWGNDSLFNKW CWENWLAICRKLKLDPFLTPYT KIHSRWIKDLNVRPKTIKTLEEN LGNTIQDIGMGKDFMTKTPKA MATKAKVDKWDVIKLKSFCTA KETTIRVSRQPTEWEKIFAIYPS DKGLISRIYKELKQIYRKK\TNN PIKKWAKNMNRHFSKEDIYAA NRQMKKCSSSLVIREMQIKTTM
4222	34590	A	4263	1	1989	
4223	34591	A	4264	1	1104	
4224	34592	A	4265	1	879	
4225	34593	A	4266	1	1659	
4226	34594	B	4267	1	1500	
4227	34595	B	4268	1	1962	
4228	34596	B	4269	1	1716	
4229	34597	A	4270	1	1152	
4230	34598	A	4271	1	4752	
4231	34599	A	4272	1	2790	
4232	34600	A	4273	1	3477	

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4233	34601	A	4274	1	1007	MLDASCHRTSDSKFFSFGVQTGFLTPELAHLVGPCDRDHNSSPAREQNWTENEFDELTEVGFRKWVITNSSELKEHVLTQSKEAKNLEKRAIKQEKEIKGIQLGKEEVKLSLFADDMIVYLENPIVSAQNLLKLISKFSKVSGYKINVQKSQALLYTNNR\SQIMSELPFTIAMKRIKYLGIQLTRDVKDLFKDNYKPLLKEIREDTNKWKNIPCSWLGRINIMKMAILPKAIYRFNAIPIKLL*TFFTELEKTTLNFIWNQKRARIAKTILSKKNKAGGITLPDFKLYHKATVTKTAWYWYQNRYIDQWNRTEASEITPHIYNHLIFDKPE
4234	34602	A	4275	737	2460	RIKYLRIQLTRDVKDLFKENYKSLLNEIKEDTNKWKNIPCSWIGRMNIIKMAI/LPKVIYRFNVIPIKLPMTFFSELEKSTLKFIWNQKRARIAKTILSQKNKAGGIMLPDFKLYYKATVTKTAWYWYQNRDIDQWNRTEPSEMTPHIYNHLIFDKPDKNKQWGKDSLFNKWCWENWLAIGRQLKLDPFLTPYTKINSRWIKDLNVRPKTIKTLEENLGNTIQDISMGKDFMSKTPKAMATKAKMDKWDLIKLKSFCTAKETTIRVNRQPTEWEKNFAIYSSDKGLISRIYKQLKQIYKKKTNNPIKKWAKDMNRHFSKEDVYAANRHMKKCSSSLAIREMQIKTIMIYHLTPVTMAIIKKSGNNRCWRGCGEMGTLLYCWWDCKLVQPLWKTLWQFLRDLELGIPFDPAIPLLGIYPKDYKSCCYKDTCTPKLARDDQIHILKQHRRKELETRQKQYRAWYEINPFHSVWPVTAGKSPRHQLPVWVHNPQTSPYLQLQTRDGEESNENNFGSTILASDFFAEIDKLSILQIHMEMEGTQNSQNNLDKKKTKMEDLHFSISKLLHSYSIQDNVISA
4235	34603	A	4276	3	355	RQPVHLVHELPQQSWGICLNSSEQHGALQHSSLHL/RMCSEPWSSADPQ*R*TCRNL*LPVRGPPRRTDLFSVSSKSTLKEWPLLLMILAELGSYLILSGRREESYFTSLVLISIGDC
4236	34604	B	4277	78	791	

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4237	34605	A	4278	1	3395	MIISIDTENAFEKIQQPFMLKTL NKLGIDGTYLKIIRAIYDKPTAN IILNGQKLEAFPLKTGTRQGCPL SPLLFNIVLEVMARVIRQEKEIK GIQLGKEEVKLSLFVDDMIVYL ENPIVSAQNLLKLISNLSKVSGY KINVQKSQAFSYTNNRQTESQI MNGLPFTTASKRIKYLGIQLTR DVKELFKENYKPLLNEKKVDT NKWKNIPCSWIGRIN\ILKMAIL P/KELEKTTLKFIWNQKRACIAK SILSKKNKAGGITLPDFKLYYK ATVTKTAWYWYQNRDIDQWN RTEPSEII\PHIYNHLIFDKPDKN KKWGMGSLFNKWCWENWLAI CRKLKLDPFLTPYTKINSRWIK DLNVRPKTIKTLEENLGNTIQDI DMGKDFMSKTPKAMATKAKID KWDLTKLRSFCTAKETTIRVNR QPKEWEKIFAIYSSDKGLISRIY KELKRIYK/KKNNPIKKWAKD MNRYF*KEDIYAANRHMKKCS SSLAIREMQIKTTMR/YHLTPVR MAIIKKSGNNRWEMNNENTWT QEGEHHTLG/HC/WWKARRSRS CLTWMAAGKKRMRKTLQMT
4238	34606	B	4279	1	2011	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Met hod	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
4239	34607	A	4280	1	2661	MTMNFVADSHTGRNPLASAAG AKTGLRPLPRPCGARVWNPPD AGGGGVGSLKTSTPLGPLSAAN SPVHQGSVPQTRARGGGTLFQE VVTSRTLAFRNSLSAFTEVTSG TVSGRKGGRSTHLAGRRVSGG EGSRKAAAAALAAVAAAPGPV RRCSSQSCFSSSGSSHYSARTSP VRVRPRRSLSSRSAAGNRAEAT ESAMEKTLETVPLERKKREKEQ FRKLFIGGLSFETTEESLRNYYE QWGKLTDCVVMRDPASKRSRG FGFVTFSSMAEVDAAMAARPH SIDGRVVEPKRAVAREESGKPG AHVTVKKLFVGGIKEDTEEHHL RDYFEEYGKIDTIEIITDRQSGK KRGFGFVTFDDHDPVDKIVLQK YHTINGHNAEVRKALSRQEMQ EVQSSRSGRGDGYGSGRGFGD GYNGYGGGPGGGNFGGSPGYG GGRGGYGGGGPGYGNQGGGY GGGYDNYGGGNYGSGNYNDF GNYNQQPSNYGPMKSGNFGGS RNMGGPYGGGIWKNTSITERK KSRKLDLIQSKKGSRTKEAPQP PVASLCMHLGHWSRLMVSPGA QLTGKNSHGLSVSSVRKSNVGP RRLCAAMKATGPDNAQSQVSP PGHAPSAEDPTGSRTVSSPCTD RPHPFLSRPKPPTQISLVLPLKT DGALERMPQQL/HIASS/GAKVP NPSTQTPPVLLAFFYPFNLPP*N
4240	34608	A	4281	1	908	MRKVKGKNRQSFKCLPPPSGA LQAHGAAAPHGSLLTLHLHLV PVSSAAMKATGPDNAQSQVSP PGHAPSAEDPTGSRTVSSPCED RPHPFLSWPTWISLALLLKTDG ALERMPQQLPSLHPSQGTQSIH PDPSSTSSFLLPFQPPTLKRAAFP CPPSIVNPAVWDTSTPSVAEHH TPIRITLKEPTQFLSQKQYPIPQA ALVGLQPIISHLLASHLLRPTDS PFNTPILPVKKPNGTYRLVQDL RLINQAVLPLVQE/DYSVLLYLP LNVTPGLPPATAFSYPPSPGPVA RARLASRLHSHAA

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4241	34609	A	4282	1	915	MPNYVTFTDTKQLISDTPNNQVPMNRASMAFDAKCLTGCRFDDAIVQFDMTYWPFTVVNDAGRPKVQVEYERDKKLLPIGGVFYGSDKDEGNCKSLPWEDCYQCCETSQNVQDFLFLDVTPLSLDIKTADGVMAVLIKCDATIPTRQTQTFTTYSDKPSM/LIAKDKNLLRKFELTGVPPAHHGAHQIEVTFDINAKGILNV\TLTDDKGHLSKEDIEPMVQETEKYKAEDEKQRDKVSSKNSLDPYVFNMKATAEDEKLQVKINNEHKQKILSKCHEIINWLDKNQTAEKEEFEHAQQELEKSS
4242	34610	A	4283	1	994	MHQTKKGNQWHFGMKAHIGVDAKSGLTHSLVTTRPNEHDLNQLGNLLHGEEQFVSADAGYQGAPQREELAEVDVDWLIAERPGKVRTLKQHPRKNKTAINIEYMKASIRARVEHPFRIIKRQFGFVKARYKGLLKNDNQLAMLFTLANLFRADQMIHCTRGEGLITTKIPKAPDNGSYCLPSKNDDSEEEDPEMSPMVVTKMKEIAEAYLGKTVTNAVLTVPAYFNDSQRQAT/KKDARTIAGLNGLRISNEPTAAAIAYGLNQKVGTERNVLIFDLGGSITPRIRTPETGSDDAIKSILEQAKKEIESQKGGECDPCRQSLRPPGPAAN
4243	34611	A	4284	3	677	
4244	34612	A	4285	30	365	EEAETVLVGQLKQLSSCLAVHKYRPETKQEKKQRLLARAEKKAAGKGDVPTKRPPVLRAGVNTVTTLVENKKAQLV\CRKMGVPYCIIKGKARLGRLVHRKTCTTVAFTQVN
4245	34613	A	4286	3	432	NSRVDDFVAAQDAKGKKVAPAPAVVKKQEAKKVVNPLFEKRPKNFGIGQ\QRLLARAEKKAAGKGDVPTKRPPVLRAGVNTVTTLVENKKAQLVVIAHDVDPIELVVFLPALCRKMGVPYCIIKGKARLGRLVHRKTCTTVAFT
4246	34614	C	4287	62	217	

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4247	34615	A	4288	2	801	PKGKKAKGKKVAPAPAVVKKQEAKKVVNPLFEKRPKNFGIGQDIQPKRDLTRFVKWPRYIRLQRQRAILYKRLKVPPAINQFTQALDRQTATQLLKLAHKYRPETKQEKKQRLLARAEKKAAGKGDVPTKRPPVLRAGVNTVTTLVENKKAQLVVIAHDVDPIELVVFLPAL\CRKMGVP\YCIIKGKARLGRLVHRKTCTT\VAFTQVNSEDKG\ALAKLVEAIRTNYNDRYDEIRRHWGGNDLRPK\SVARIAKLEKAKAKELATKLG
4248	34616	B	4289	1	273	
4249	34617	A	4290	1	441	
4250	34618	B	4291	47	482	
4251	34619	A	4292	1	762	
4252	34620	A	4293	1	890	MSKSESPKEPEQLRKLFIGGLSFETTDESLRSHFEQWGTLTDCVVMRDPNTKRSRGFGFVTYATVEEVDAAMNARPHKVDGRVVEPKRAVSREDSQRPDYFEQYGKIEVIEIMTDRGSGKKRGFAFVTFDDHDSVDKTVIQKYHTVNGHNCEVRKALSKQEMASASSSQRGRSGSGNFGGGRGGGFGGNDNFGRGGNFSGRGGFGGSHGGGGYGGSGDGYNGFGNDGSNFGGGGSYNDFGNYNNQSSNFGPMKGGNFGGRSSGPYGGGGQYFAKPRNQ/GGYGGSSSSSYGSGRRF
4253	34621	A	4294	1	1674	
4254	34622	A	4295	1	506	KYHTVNGHNCEVRKALSKQEIASASCSQRGRSGSGNFGGDRGGGFGGNDNFGRGGNFSGHGGFGGSCCGGGYGGSGDGYNGFGNDASNFGGGGS/YNEFG/NYNNQSSHFGPLS/GGNFGGRSS/SPLGGAPASTYVKGPNSQRTQNEGWFEG*APWRGDGGARGNKGGGA

SEQ ID NO:	SEQ ID NO: of peptide sequence	Met hod	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
4255	34623	A	4296	1	1445	MKCLKFINHKEILEASERKQAE SLDFPFKKLRWHLCEGWIEEER DESRKSETIFKDLFKVPVLKETI YYKFYGPPVYQIETVYFMALSP PKSKQFDKTKQNNNNKKTHQF VIVFFKTDEHLSARGRRRRSIVK VSLLPAVIGLKSKFLKKPDQLR KLFI\GG\LSFETT\DESLEEPFSR QWGKRYTDSVVMRDPNTKRSR G\FGFVTYAT\VEEVDAA\MNA RPHKVEWKELLEPKRA\VSRED SQRPGCPH*LVKKIFVGGIKEDT \EEHHLRDYFEQYGKIEVIEIMT D\RGSGKKRGFAF\VTFD\DHD\S VDKIVI\QKYHTVNG\HN\CEV* KSPVKSKKMASASSKPKEGRSG FWETFGGGSWEVGFGGN\DNF GRG\GNFSWSVVAFGGSRG\GG GYG\GSGDG\YNGFGNDG\SNF G\GGG\SYNDFG\NYNNQ\SSNF GPMKGG\NFG\GRSSGPYG\GGG QYF\AKPR\NQGGYGGSSSS\SN
4256	34624	A	4297	1	920	DPGDTPNTASAPNCRSGKGRSS SPEHIPPLEKLEDSMQTNPSTNP EPGRLAEWLDPEERQQSLQFGL QEATSIGKGGQYYIKGTPHGTK ESEQQPSALDLPSDRAYPNEKE PENQLWRLVIKLIKEAPEKGAY LNVIKAVYDKPTNGEKLRAFPL RTGTKHRCPLSPLLFNILLEVLA RAIRQEKEIKSIQIGKEEVKLSLF ADDIIIYLESPKYSSRKLQELIKE FSKVSRYEINVHKSVALLYT\NS NQAENQIKNSASFTIAAKNKIK YLGIYLTKDAKDGYKENYKTL MKEIIDDKNKQKYIP
4257	34625	A	4298	1	1194	
4258	34626	A	4299	3	1834	
4259	34627	A	4300	285	502	
4260	34628	B	4301	77	1306	
4261	34629	A	4302	1	354	
4262	34630	A	4303	1	1182	
4263	34631	B	4304	1	1995	
4264	34632	B	4305	1	1518	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Met hod	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
4265	34633	A	4306	1	918	MCPVGPWTHPVVISPVSECIVGI DILGSWQNLHIGSLTDITMVHYI DDMMLIGSSEQEVANSLDLLV RHLHARGCKINPTKIQGTSTSV KFLEFQWCGVCQDIPSKWVLE QKALQQVQAAVQAALPLEPYD PADPMVLEVSVADGVAVWSL WQAPIARIHGSRNQGVEVEVSP LTNIPSDPLAKFLFPAPSTLCSA GLELLVPEGGTLLPGNTTMIPL NWKLRLVPGYFGLLLALSPQA KNGVTVLAEVIDPDYQDEITLL FHNGGGEEYARNTGDPLRHLL VLPSPMIKVNGK\LQHPNPGRT
4266	34634	B	4307	1	1599	
4267	34635	B	4308	1	1569	
4268	34636	A	4309	3	422	
4269	34637	A	4310	1	1089	
4270	34638	A	4311	2	549	LKMTAMQRPMEKRMMNREIIL KERLSLTGIDIKILKKRSIMKVE SHRGEQISVSSLALQRIKYLGIQI TRDVKDLFKENYKPLLNKLKE DTNKWRNVPCPRVGRISIVKM AILPK/ILKKKTTLKFIWNQKRA HIAKTILSKKNKAGGITLPDFKL YYKAT/KTAWCWYQNRDTDQ WNRTKPSEI

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
4271	34639	A	4312	371	3036	LIAYQPKKVQDQMDSQPNSTRVLEVLARAIRQEKEIKGIQLGK/EEVKLSMFADDITAYLENPIVSAPNLLKLISNFSK/VSGYKINVQKSQAFLYTNKRQTE\QIMSELPFTVASKRIKYLGIKLRRDVKDLFKENYKPLLNEIKEDTNKWKNIPCSWIGRINIVKMTILPKVIYRFNAIPIKLPMTFFAELEKTTLKFIWNQKRAHIAKTILSQKNKAGGIMLPDFKLYYKATVTKTAWYWYQNRDIDQWNRIEPSEIIPHICKHLIFDKPDKNKKWGKDSLFNKWCWENWLAICRKLHLDPFLTPYTKINSRWIKDLNVRHKTIKTLEENLGNTIQDIGMGKDFMTKTPKAMATKAKIDKWDLIKLKSFCTAKETTIRVNRQPTEWEKIFATYSSDKGLISRIYNELKQIYKKKTNNPIKKWAKDMNRHFSKEDIYAAKKHMKKCSSSLAIRETLYNDRRIGKLTQTCDETAFQPHVCTISRPMLSSPYRSSLTEKWSQDFSKPPYPFLFHKGYLNPREQDKEVLTRAIRQEKERKGIQLGKEEVKLSLFADDMIVYLENPIVSAQNPLKVVSNFSKVSGYKISVQKSQAFLYTNNRQTESQIMSELPFTIASKRIKYLRIQLTRDVKDLFKENCKPLLNEIEEDTNKWKNIPCSWIGRINIVKMAILPKVIYRFNAIPIKLPMTFFTVLEKTTLKFIWNQKRAH
4272	34640	B	4313	1	1995	
4273	34641	A	4314	3	549	
4274	34642	A	4315	3	614	EAYGQTECTGGCTFTLPGDWTS\GQFINILEMCLELSPCKSFSADSARYVLGHVGVPLACNYVKLEDVADMNYFTVNNEGEVCIKGTNVFKGYLKDPEKTQEAL\DSDGWLHTGDIGRWLPDIENHNRLIVCTLTNTSWRSHKIIVLKTYQKADDTKTPKETTFQNIMNLFLKEKRATAVLIRGGVGETSTDLSKKKPAKLLANF
4275	34643	A	4316	1	478	MKLDLHLSPYTKINSRWIKDLNLRPETIKILEDIIRKTLLDIGLGKDFMIKNPKVNATKTKINKWDLIKLK\NFCTAKEISSREIREPTEWEKIFANSASDKGLISRIYKELKQIRSTLQLLFGISELPASLFLGFGAIMKSKKASLNTSTAILRQLIW

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4276	34644	A	4317	1	1125	MCHGIGAQIIPSHQTVQLDITAFLKTVKKNKHKFYPAFIHILARLMNAHPEFRMAMKDGFIENMFFVSANPWVSFTSFDLNVANMDNFFAPVFTMGKYYTQGDKVLMPLAIGGPLESPDRDGGPLESTNRDASPESWSCRKSTPRLVAWVSAAKVFIRDKLMERRNRRTGRTEKARIWEVTDRTVRTWIGEAVAAAAADGGGFRVDLARRSIRKDRNARSQNPVHTEGDMNMNIKKIVKQATVLTFTTAFLAGGATQAFAKENNQKAYKETYGVSHITRHDMLQIPKQQQNEKYQVPQFDQSTIKNIESAKGLDVWDSWPLQNADGTVAEYNGYHVVFALAGSPKDADDTSIYMFYQKVGDNSID\SWKNAGRVF
4277	34645	B	4318	1	1374	
4278	34646	A	4319	1	1293	
4279	34647	A	4320	1	1278	
4280	34648	A	4321	1	1254	MNMNIKKIVKQATVLTFTTALLAGGATQAFAKENNQKAYKETYGVSHITRHDMLQIPKQQQNEKYQVPQFDQSTIKNIESAKGLDVWDSWPLQNADGTVAEYNGYHVVFALAGSPKDADDTSIYMFYQKVGDNSIDSWKNAGRVFKDSDKFDANDPILKDQTQEWSGSATFTSDGKIRLFYTDYSGKHYGKQSLTTAQVNVSKSDDTLKINGV\NGYYCEES\LFNKA\YYGGGTNFFRKESQKLQQSAKKRDAELANGALGIIELNNDYTLKKVMKPLITSNTVTDEIERANVFKMNGKWYLFTDSRGSKMTIDGINSNDIYMLGYVSNSLTGPYKPLNKTGLVLQMGLDPNDVTFTYSHFAVPQAKGNNVVITSYMTNRGFFEDKKATFAPSFLMNIKGNKTSVVKNSILEQGQLTVN
4281	34649	A	4322	1	726	
4282	34650	A	4323	1	1050	

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4283	34651	A	4324	1	1185	MNMNIKKIVKQATVLTFTTALLAGGATQAFAKENNQKAYKETYGVSHITRHDMLQIPKQQQNEKYQVPQFDQSTIKNIESAKGLDVWDSWPLQNADGTVAEYNGYHVVFALAGSPKDADDTSIYMFYQKVGDNSIDSWKNAGRVFKDSDKFDANDPILKDQTQEWSGSATFTSDGKIRLFYTDYSGKHYGKQSLTTAQVNVSKSDDTLKINGVEDHKTIFDGDGKTYQNVQQFIDEGNYTSGDNHTLRDPHYVEDKGHKYLVFEANTGTENGYQGEESLFNKAYYGGGTNFFRKESQKLQQSAKKRDAELANGALGIIELNNDYT\LKKVMKPLITSN/TVPQAKGNNVVITSYMTNRGFFEDKKATFAPSFLMNIKGNKTSVVKNSILEQGQLTVN
4284	34652	B	4325	1	867	
4285	34653	A	4326	1	495	
4286	34654	A	4327	3	1394	GDMNMNIKKIVKQATVLTFTTA/LLAGGATQAFAKENNQKAYKETYGVSHITRHDMLQIPKQQQNEKYQVPQFDQSTIKNIESAKGLDVWDSWPLQNADGTVAEYNGYHVVFALAGSPKDADDTSIYMFYQKVGDNSIDSWKNAGRVFKDSDKFDANDPILKDQTQEWSGSATFTSDGKIRLFYTDYSGKHYGKQSLTTAQVNVSKSDDTLKINGVEDHKTIFDGDGKTYQNVQQFIDEGNYTGDPLEAETAVINHKKRKNSPRIVQSNDLTEAAYSLSRDQKRMLYLFVDQIRKSDGTLQEHDGICEIHVAKYAEIFGLTSAEASKDIRQALKSFAGKEVVFYRPEEDAGDEKGYESFPWFIKRAHSPSRGLYSVHINPYLIPFFIGLQNRFTQFRLSETKEITNPYAMRLYESLCQYRKPDGSGIVSLKIDWIIERYQLPQSYQRTPDFRRRFLQVCVNEING
4287	34655	B	4328	9	1004	
4288	34656	A	4329	1	768	
4289	34657	A	4330	1	1308	
4290	34658	B	4331	58	753	
4291	34659	B	4332	1	409	
4292	34660	B	4333	1	921	
4293	34661	A	4334	1	1026	
4294	34662	B	4335	1	945	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Met hod	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
4295	34663	A	4336	1	528	MNMNIKKIVKQATVLTFTTALLAGGATQAFAKENNQKAYKETYGVSHITRHDMLQIPKQQQNEKYQVPQFDQSTIKNIESAKGLDVWDSWPLQNADGTVAEYNGYHVVFALAGSPKDADDTSIYMFY/QKDQTQEWS\GSATFTSDGKIRLFYTDYSGKHYGKQSLDTA\Q*NVVKSG
4296	34664	A	4337	1	1701	
4297	34665	B	4338	97	1449	
4298	34666	A	4339	1	1581	
4299	34667	B	4340	1	1539	
4300	34668	A	4341	87	1078	SLPNLDNAAICSSSSSPTRTR*SLSEGATQ\AFAKEKYPHKHTKKRSGVFHITRHDMLQIPKQQQNEKYQVPQFDQSTIKNIESAKALDVWDSWPLQNADGTVAEYNGYHVVFALAGSPKDADDTSIYMFYQKVGDNSIDSWKNAGRVFKDSDKFDANDPILKDQTQEWSGSATFTSDGKIRLFYTDYSGKHYGKQSLTTAQVNVSKSDDTLKINGVEDHKTIFDGDGKTYQNVQQFIDEGNYTSGDNHTLRDPHYVEDKGHKYRGPLESPSTHQAEFNPTSCVSSLGTLQGFPAPAWLALAHPVHPLKHKSGGSNRLSAAIWGIKRKPAR
4301	34669	A	4342	1	1344	
4302	34670	A	4343	1	1713	
4303	34671	A	4344	3	1918	
4304	34672	A	4345	254	1118	RPPAFAKK*PKAYKET/YGVSHITRHDMLQIPKQQQNEKYQVPQFDQSTIKNIESAKGLDVWDSWPLQNADGTVAEYNGYHVVFALAGSPKDADDTSIYMFYQKVGDNSIDSWKNAGRVFKDSDKFDANDPILKDQTQEWSGSATFTSDGKIRLFYTDYSGKHYGKQSLTTAQVNVSKSDDTLKINGVEDHKTIFDGDGKTYQNVQQFIDEGNYTSGDNHTLRDPHYVGGTSWEPGVFSVSCVFFGQQEGV/HG*DEFLDFSYWFQGG*ICLYQKAS*QNTTSYKRYTGS

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
4305	34673	A	4346	1	1952	MNMNIKKIVKQATVLTFTTALLAGGATQAFAKENNQKAYKETYGVSHITRHDMLQIPKQQQNEKYQVPQFDQSTIKNIESAKGLDVWDSWPLQNADGTVAEYNGYHVVFALAGSPKDADDTSIYMFYQKVGDNSIDSWKNAGRVFKDSDKFDANDPILKDQTQEWSGSATFTSDGKIRLFYTGSLNSSKTEKYQVPHIDQSTIKNIESAKGLDVWDSWPLQNADGTVAEYNGYHVVFALAGSPKDADDTSIYMFYQKVGDNSIDSWKNAGRVFKDSDKFDANDPILKDQTQEWSGSATFTSDGKIRLFYTDYSGKHYGKQSLTTAQVNVSKSDDTLKINGVEDHKTIFDGDGKTYQNVQQFIDEGNYTSGDNHTLRDPHYVEDKGHKYLVFQDHTGTEEHPQPQ\ERPRTQSFTSAFAERRECIPNVPADTKLSKIKTLRLATSYIAYLMDLLAKDDQNGEAEAFKAEIKKTDVKEEKRKKELASKCLDLEQLGASVEPTGNLRTKITKEKPRHTGPPEVVVPGCCPHRSRAYKSDKYAHTLTVTASQHAPPPTHMEGFELFHLPDLCSPSQDAQTTGRTQMKPDHSPRPSHRVPQAKGNNVVITSYMTNRGFFEDKKATFAPSFLMNIKGNKTSVVKNSILEQGQLTV
4306	34674	A	4347	1	1029	
4307	34675	A	4348	276	1248	CVWLGCRGYYPKAYKETY\GVSHITRHDMLQIPKQQQNEKYQVPQFDQSTIKNIESAKGLDVWDSWPLQNADGTVAEYNGYHVVFALAGSPKDADDTSIYMFYQKVGDNSIDSWKNAGRVFKDSDKFDANDPILKDQTQEWSGSATFTSDGKIRLFYTDYSGKHYGKQSLTTAQQLLQLVQFQEVDTDFDFPEEDKKEEFEECLEKFFSTGPARPPTKEKVKRRVLIEPGMPLNHIEYCNHEIMGKNVYYKHRWVAEHYFLLMQYDELQKICYNEFVPSVIFLRYKSPGEAAGTCHLKQRRWVMPEAAAPVGTGSRYPLTGQL
4308	34676	A	4349	1	242	MNSIQIPKQQQNEKYQVPQFDQSTIKYIESPKELDVWDSWPLQNADGTVAEYNGYHVAFALAG/SPKDADDTSIYMFYQKI
4309	34677	B	4350	1	2198	

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4310	34678	A	4351	1	2796	
4311	34679	A	4352	2047	3531	
4312	34680	A	4353	1	3336	
4313	34681	A	4354	1	1409	MKRAPVIPKHTLNTQPVEDTSLSTPAAPMVDSLIARVGVMARGNAITLPVCGRDVKFTLEVLRGDSVEKTSRVWSGNERDQELLTEDALDDLIPSFLLTGQQTPAFGRRVSGVIEIADGSRRRKAAALTESDYRVLVGELDDEQMAALSRLGGATQAFAKENNQK\AYKETYGVSHITRHDMLQIPKQQQNEKYQVPQFDQSTIKNIESAKGLDVWDSWPLQNADGTVAEYNGYHVVFALAGSPKDADDTSIYMFYQKVGDNSIDSWKNAGRVFKDSDKFDANDPILKDQTQEWSGSATFTSDGKIRLFYTDYSGKHYGKQSLTTAQVNVSKSDDTLKINGVEDHKTIFDGDGKTYQNVQQFIDGYLLEPDGGALQNFQRYTGIQHVHRIGMAERMWCDRNRERHTVSSSGGNRLPNPGPDRSVRHFPDPRFLCPSCATVTPLHELIANKYLSGKIGAKKLRKLLIKHVD
4314	34682	A	4355	1	2316	
4315	34683	A	4356	93	924	AQTDAAEKSVSIAQLFQACLSIFSSGDV/AGGATQAFAKENNQKAYKETYGVSHITRHDMLQIPKQQQNEKYQVPQFDQSTIKNIESAKGLDVWDSWPLQNADGTVAEYNGYHVVFALAGSPKDADDTSIYMFYQKVGDNSIDSWKNAGRVFKDSDKFDANDPILKDQTQEWSGSATFTSDGKIRLFYTDYSGKHYGKQSLTTAQVNVSKSNDTLKINGVGKYKTIFDGDGKTYQTVQQFIDEGNYTSGGHHTL\KDPSYNPPLDLSGGNSGYQSQET

SEQ ID NO:	SEQ ID NO: of peptide sequence	Met hod	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
4316	34684	A	4357	1	3118	MNMNIKKIVKQATVLTFTTALL AGGATQAFAKENNQKAYKETY GVSHITRHDMLQIPKQQQNEKY QVPQFDQSTIKNIESAKGLDVW DSWPLQNADGTVAEYNGYHV VFALAGSPKDADDTSIYMFYQ KVGDNSIDSWKNAGRVFKDSD KFDANDPILKDQTQEWSGSATF TSDGKIRLFYTDYSGKHYGKQS LTTAQVNVSKSDDTLKINGVED HKTIFDGDGKTYQNVQQFIDEG NYTSGDNHTL\RDP\HYVENKG HKYLGFETNTGTENGYQGEESL FNKAYYGGGTNFFRKESQKLQ QSAKKRDAELANGALGIIELNN DYTLKKVMKPLITSNTVTDEIE RANVFKMNGKWYLFTDSRGSK MTIDGINSNDIYMLGSDESPND FGNRHLHKERLAVYRWHASFI CSGNTMPIVLVDWSDIREQKRL MVLRASVALHGRSVTLYEKAF PLSEQCSKKAHDQFLADLASIL PSNTTPLIVSDAGFKVPWYKSV EKLGWYWLSRVRGKVQYADL GAENWKPISNLHDMSSSHSKTL GYKRLTKSNPISCQILLYKSRSK GRKNQRSTRTHCHHPSPKIYSA SAKEPWVLATNLPVEIRTPKQL VNIYSKRMQIEETFRDLKSPAY GLGLRHSRTSSSERFDIMLLIAL MLQLTCWLAGVHAQKQ
4317	34685	A	4358	1	1326	
4318	34686	A	4359	2140	4390	
4319	34687	B	4360	1	7271	
4320	34688	A	4361	1	1729	
4321	34689	A	4362	5118	5687	
4322	34690	B	4363	1	4726	
4323	34691	B	4364	1	3688	
4324	34692	A	4365	1	1401	
4325	34693	A	4366	1	1932	
4326	34694	A	4367	1	1407	
4327	34695	A	4368	1	1491	
4328	34696	B	4369	1	855	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
4329	34697	A	4370	137	1014	ASEGKQMLRDFVTTRSALKELL KRALNMARNNQYQPLQKHAK L*RPSML*RNCIN*QPGRDT/TN KKENFRPISLMNIDAKILNKILA NRIQQHIKKLIHNDQVGFIPGM QGWFNIHKSINIIHHIKRTNDKN HMIISIDAEKAFNKIQQPFMLKT LNKLGIDGTYLKIIRAIYDRPTA NVILNGQKLEAFPFKTGTRQGC PLSPLLFNIVLKVLARAIRQETEI KGIQLAKEEVKLSLFADDMIVY LENPIISAQNLLKLISNFSK/VSG YKINVQKSQAFLYTINRQTESQI
4330	34698	A	4371	3	1234	
4331	34699	A	4372	1	2850	MGMGPAKPGMGGNLLVCWLQ RPWEKRSIWAEVYRSSRYSHS WLPLSRKGCDFSGTCRQTLSIL TQPLRQWGLEGIKKPNSWIISEE SVSNGGPPLLIPRQTASGVDLQ QTPTDLQLRVLTVRRKTNKQK GIASTSTKRTSTPKPHLYVTIIK DQSYIKPQRWGKNIAEKLKILKI RVALSLQRNAAPHQQWNKAG RRMSLMSSQKKASEVIESQMN EIKGEEKFREKRVKRNEQSLQEI WDYVKRPDLRLIGVPD
4332	34700	B	4373	16	701	
4333	34701	B	4374	1	3743	
4334	34702	A	4375	227	686	KVMLAEYPVFAQLTLTLPPSSA SWEPSRGPGPRGIRGSCPEWLA SGPG\KAAPGAGVPPPAASFPDP PPRLRAPALAVSRGLRRELPSG LDWTHCLRTLPSLIVQILQQAA LLGLPPAYSDQLQRAGQLHFYS GLIKISLVLTTRLSFWGTTE
4335	34703	A	4376	216	644	VTYSKEKECGEVADSVAKTAL EKDGAPRTGDPRPNLGADPPRS LVSSAGPQAVRPVKPARQFPPQ PPRYSQGPARAAGEEGRGMRPP GAGRRLPGPPLPGPEASHSGQL PLM/PPGPGPRLGSQEPVSLSRY LQTQARMPGPRP

SEQ ID NO:	SEQ ID NO: of peptide sequence	Met hod	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
4336	34704	A	4377	18	1023	QIQHSPLVSPLPSLPPQPLVAEE EPPVA/PWPRRLLPATSTSH/PSH PLTEPVPPT\SGRGCCLWTKRQ QKMCRTTYTSVGRK/CTFPIDS GALRLSDGEMRALQTPTGPQST VEGHTHLQSL/PHHDRVTATPG TEPGLRAAGNRRIFYPGP/VTSQ VQPQLLCGYGNASRTPAALTPG PAPPTQASLPNCGICPHLQMGR PTSPC/PPEGGHPSSSLYISLSPPP PSAPALRLPPPLP\SAPTAPAL/P/ PAAPSAPALRLLRPLPCCSFRPR PAAPSAPAPRLLPPLLVCSFRPC PAAPSAPAGLLLPPLLCCSGLSP RLCCPHSSCSSDPPRLQRKADSS
4337	34705	B	4378	1	984	
4338	34706	A	4379	332	847	VKLLLQDKEICILCQKTVYPME CLVADKQNFHKSCF\RCHHCNS KLSLGNYASLHGQIYCKPHFKP TFQNPKGNYDEGFGHKA\HKD RWNWQKPKADSVDFIPNEEPN MCKNIAENTLVPGDRNEHLDA GNSEGQRNDLRKLGERGKLKV IWPPSKEIPKKTLPFEEELKMSK
4339	34707	A	4380	305	505	GNLERMLNLGMVKQQKLPAIM KTQVLML*AINVPAKPLFPQSG GAVRTTHGGKSRLKETGATSD TE
4340	34708	A	4381	56	260	IVKTQSIDG/MGNLRITEKGLKL EGDS/EFLQPLYAKEIQSRPGLG TQEQSCQTLSSCSSRGQQQHAE
4341	34709	A	4382	137	920	
4342	34710	A	4383	532	1680	LLTTRTSFRSENHRHVGLLLVM TDNTRDKEYFGDESKRENEEKT VEKSIGEKQATLTTHANIITIRH CVKPEPDFSDHLNLLLGRADIT GEEMAAQRSSVEKLANGNIAL VDSLRSRSLEEGDSDPHKRLSG AQDIKTTVEEVIADVVEIARELE LEVEPEDVTEFLQAHEKTLTDV ELFLINEQIKWFLEMKSTPRED AVIIAETITKVLEYDINLVTKQQ QGMRQLTPILKEVLLWVKCHQ TALHATEKPFIKGRINPCGKIHT CLNLRNCGQLLIREEEEEDKEE EEQYEEKEEEEEEEEEEEEEEE EEEEEEEEEEEEEEEDEEEEDKE DEEEDKEKEEEEDNKEEEEEED KEKEEEEDKE\EKEDKEEEEDK

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4343	34711	A	4384	3	495	EDTGTFRIY\ESAGAVKKARGFLEFVEDFIQVSKNLIGKVIGKNGKVIQEIVDKSDMVPVRIEGDSENKLPREDKDDRDSRHQRDSRRCPGGRCRSVSGRRGRGGPRGGKSSISSVPKDPDSNPYSVLDN/TESDQTADTDASKSHHSTNRHTRSRRRRTDEDAVL
4344	34712	A	4385	1	550	TESERKDELSDWSLAGEDDRDSRHQRDSRRRPGGRGRSVSGGRGRGGPRGGKSSISSVLKDPDSNPYSLLDNTESDQTADTDASESHHSTNRRRRSRRRRTDEDAVLMDGMT\ESDTASVNENGL\AKDVIEEHGPSEKAINGPT\SASG\DDISKLQRTPGERKRLIP*KKENTQEAAVLNGVS
4345	34713	A	4386	1	2063	MAELTVEVRGSNGAFYKGFIKDVHEDSLTVVFENNWQPERQVPFNEVRLPPPPDIKKEISEGDEVEVYSRANDQEPCGWWLAKVRMMKGEFYVIEYAACDATYNEIVTFERLRPVNQNKTVKKNTFFKCTVDVPEDLREACANENAHKDFKKAVGACRIFYHPETTQLMILSASEATVKRVNILSDMHLRSIRTKLMLMSRNEEATKHLECTKQLAAAFHEEFVVREDLMGLAIGTHGSNIQQARKVPGVTAIELDEDTGTFRIYGESADAVKKARGFLEFVEDFIQVPRNLVGKVIGKNGKVIQEIVDKSGVVRVRIEGDNENKLPREDGMVPFVFVGTKESIGNVQVLLEYHIAYLKEVEQLRMERLQIDEQLRQIGMGFRPSSTRGPEKEKGYATDESTVSSVQGSRSYSGRGRGRRGPNYTSGYGTNSELSNPSETESERKDELSDWSLAGEDDRDSRHQRDSRRRPGGRGRSVSGGRGRGGPRGGKSSISSVQYRSNIHNCSTLKRIFLASDMNIVLKDPDSNPYSLLDNTESDQTADTDASESHHSTNRRRRSRRRRTDEDAVLMDGMTESDTASVNENGLDDSEKKPQRRNRSRRRRFRGQAE\DRQPAIDFIYKEVEKVVSLWQAKDVIEEHGPSEKAINGPTSASGDDISKLQRTPGEEKINTLKE

SEQ ID NO:	SEQ ID NO: of peptide sequence	Met hod	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
4346	34714	A	4387	1	1882	CGSNMADVTVEVRGSNGAFYKGFIKDVHEDSLTVVFENNWQPERQVPFNEVRLPPPPDIKKEISEGDEVEVYSRANDQEPCGWWLAKVRMMKGEFYVIEYAACDATYNEIVTFERLRPVNQNKTVKKNTFFKCTVDVPEDLREACANENAHKDFKKAVGACRIFYHPETTQLMILSASEATVKRVNILSDMHLRSIRTKLMLMSRNEEATKHLECTKQLAAAFHEEFVVREDLMGLAIGTHGSNIQQARKVPGVTAIELDEDTGTFRIYGESADAVKKARGFLEFVEDFIQVPRNLVGKVIGKNGKVIQEIVDKSGVVRVRIEGDNENKLPREDGMVPFVFVGTKESIGNVQVLLEYHIAYLKEVEQLRMERLQIDEQLRQIGSRSYSGRGRGRRGPNYTSGYGTNSELSNPSETESERKDELSDWSLAGEDNRDSRHQRDSRRRPGGRGRSVSGGRGRGGPR\GGKSSISSVLKDPDSNPYSLLDNT\ESDQTADTDASESHHSTNRRRR/SIRRRRTD\EDAVLMNGMTESDTASVNENGLVTVADYISRAESQSRQRNLPRETLAKNKKEMAKDVIEEHGPSEKAINGPTSASGDDISKLQRTPGEEKINTLKEENTQEAAVLNGVS
4347	34715	A	4388	2	421	PRVRDSDTEDDSEAEHFESFIHPTAMMFTSTINLLQTLCLSAGVHAEIMQSEATKTLCGLL\KSSPNRLVYREQHRSWCTLGFVQSIALTLQVCGALSSLQWITLLMKVVEGHAPFTATSLQRQILAVHLLQAVLPSWDK
4348	34716	A	4389	269	417	DLNCKVGSCFEVYSS*KQGIN*IKLGDSKT*P*LSGPTSENLKNSSLAE
4349	34717	A	4390	1	516	
4350	34718	C	4391	1	1527	

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4351	34719	A	4392	200	1267	TFSKASRGGNPHSMTKAPSDFR KARQTGIPGCSQLGSRYSLEPE QSALRLVCIQKLQESSTTCEDFF CPLCGRAWAVSTPLTDSPSPGH QPAVK*LGLVPFSDTHHPLPFQ VLSTDDTSSSSSCSSSCSASSSSP /SLLLLLLFLLLLLLLLMLLLKL FLLLLLFLL/RPPASPPLLPPALS PPL/HCSSSPSAPPASPPPAPPPPP APPPSPPPAPPPSAPSSPAPLPPA PASPPFSCSSSSCSSSCSSSSFSSC SSLSSSAQAEGSLRAPRESSPSL DPSAPQRVKVVPPQAGSGHRA GGALENRPRGKKPWLHFRPGL RSRLPARSLRSRPAPTRWRLRSS GRFTGAATATATART
4352	34720	A	4393	1	2607	MMGHSSAIPLTATPGELKGQSP TKMPDPELGCQGAKSQGCSRN ARHQKARSMPLQDQHLALAIL LELAVQRGTLSQMLSAILLLLQ LWDSRAQETDNERSAQGTSTL LLSLLQTFQSIICSKDTPPSEGN MHLLSGPLSPSESFLRESFFTVQ NCRNNEEVTLICKADLENHNK DGGFWIVIDEKVYDIKDFQTQS LTGNSILAQFAGENPVVALEAA FEFEVTRESMHAFCVGQYLEVR LYALSDAEDGRG\TL*WLQSSIF SG/GLQTSQIHYSYNEEKDEDH CS/SPVGTPASKSR\CSHRWALG DHSQAFLQAIADNNIQDHNVKT HQEQGRSYKEVCTPVIERLRFL SNELRPAVGNDLSIISEFKLLSSL PRWRRIAQKIIRERRKKRIPKKP ESTADEEKIGNEESDLEEACILP HSPINVDKRPIAIKSPKTITSENP LGPSLGSIPQARFLLMMLSMLT LQHSANNLDLLLNSGTLALTQT ALRLIGPSCDNVEEDMNASAQ GVSATVLEATRKETAPVHLPVS GPELAATMKIGTRVMRGVDW KWGDQDGPPPGLGRVIGELGE DGWIRVQWGTGSTNSYRMGK EGKYDLKLAELPAAAQPSAEDS DTEDDSASPNRLVYREQHRSW CMLGFVRSIALTPQVCGALSSP QWITLLMKVMKGHAPFPAASL QRQRWVAVSLPHALVKSGTVP

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4353	34721	A	4394	266	1110	WARGGCARNALASGNAIQGGKCNPGLFPPSPNRLVYREQHRSWCMLGFVRSIALTPQVCGALSSPQWITLLMKVMKGHAPFPAASLQRQLCPE/HTSCPVLKDFCKSVITDVACSSLISTLLVFWGGLLHTHKEASESWREAKSTSYVAAARENEEDAKAEPPTPGIKPSDLVRLIHYQENSMGETAPMIQIISHWVPPTTHGIYGSTIQDEIRVGVSYPGHTDARGFQLLLVSGDFSIPYWSLSSAYTSVNSSFVESLQSNLLKGILLPATIMTDPRTTGHQ
4354	34722	A	4395	1	734	MVQLSGKRILNSPYLELRCHQNMDHLGWVIKKSLNRSEVSWVPGLEFPWGPKPFREVIAGPLLRNNGQSLESSSLEGSHVGVYFSAHWCPPCRSLTRVLVESYRKIKEAGQNF\EIIFVSADRSEESFKQYFSEMPWLAVPYTDEARRSRLNRLYGIQAHLFLTANAEDFDTTVQVNKIILITYRQNENSLSSLKTGETEAQGRLQGSPSNVRGHDPDRHAIPLSVNRWNPSKSSPSPAVWS
4355	34723	A	4396	195	1071	LHEFDSSRDLTSGLGGARTHRRLGGPSDAPRGLPAPPPAPPVRPG/PRSPGPSAGTAR/DAPRPSVQMRAQRPARGSTKDLIETCCAAGQQWAIDNDECLEIPESGTEDNVCRTAQRHCCVSYLQEKSCMAGVLGAKEGETCGAEDNDSCGISLYKASLTCGLQGRCLNPQQASMGLFSYDVQSSKKINRSIQEKLGGHGVCAATPGGGMRNCGRLRRSGQRRGGTDRCEAVLTGLFTRALIREQMGDPHPLDHTGQLAKPLEVEKTPARWKYLDTNGEKEEPELRTQCPSLYED
4356	34724	A	4397	1	520	MMGEKAEKPDTKEKKPKAKKADAGGKRNCRYSRSAMYSRKTTSRKKYSAAKSKVEKKKKFLATVTKPVGVDKNSGTQVVKLHKMPRYYPTEDVPLKLLSHG/KKKPFSQHR/RRVVFLKQLV/SGTGPLVLNQVPLRRTHQKFVIATSTKIGSSNVKIAKRLTGAYFKKVWKPKHQE
4357	34725	C	4398	67	243	

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4358	34726	A	4399	1	333	QRSCIENILRAC/VGLPPQNHMLLEHKM\DAKRVGPVAATYPMLNKKGPVPAATNGCTGDANGHLQEEPPMPTT*GPGHTVSRLFLPAAPHDPTLKAPTNNSAATQPSKNKKK
4359	34727	A	4400	587	1013	GAASAGRGPGPRAPGLWGRGPAAAGASLVPTDHVHLSYNHLGNNDGENLSAP/SQFRSKEVSKSNVVDD/MVQSNPVLYTPGEEPDHATRCWPHPSAGPSAADRAVPARPAGAPATEPHAPGTQNGAPGPSLKRVGPVAATYPI
4360	34728	A	4401	2	334	
4361	34729	B	4402	257	975	
4362	34730	A	4403	30	365	EEAETVLVGQLKQLSSCLAVHKYRPETKQEKKQRLLARAEKKAAGKGDVPTKRPPVLRAGVNTVTTLVENKKAQLV\CRKMGVPYCIIKGKARLGRLVHRKTCTTVAFTQVN
4363	34731	C	4404	62	217	
4364	34732	A	4405	2	69	
4365	34733	A	4406	1	951	GTRPKMPKGKKAKGKKVAPAPAVVKKQEGFRKKW*IPWFEKRP\KNFGIGQDIQPQKRPPPLL*KWPRQYQACSGQRAILYKR\LKVPPAMKPVSPRALD\RQT\ATQLA*AVAHKVQTQRQKQEKKQRL\LARADEEGCLAKGDVPNERDPPVPSSQEFNPVSPPLVKEQEKLKLVVNWHTDV\DPHPSLVCLPC/LCPAPVS*KMGGPFTCIIQGKRARLWDRLVPQERPCTTCPPFT\QVN\SEDKVRLLAKAGLEAIQGPIYN*PDTMEIRPSLGVGNVLG\PKSVARI\AKARNRHKAKETATHTGLNVTLLSFLYYKNN

SEQ ID NO:	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
4366	34734	A	4407	1	1392	MPDVSEEQKESVCTGSMMREE ESSRKGKVRTAGAKSSSSDRVP RLNQEEVESLNRPITGAEIVAIIN SLPTKKSPAPDGFTAEFYQRIRI QQPIIRIQQPIKKLIQHDKVGFIP GMQGWFNICKSINVIQHINRTK EKNHMIISIDAEKPFDKIQQCFM LKTLNKLGIDGTYLKIIRAIYHK PTANIILNGQKLEAFPLKTGTRQ GCPLSPLLFNIVLEVLARAIRQE KEIKGIQLGKEEVKLSLFADDM IIYLENPTVSAQNLLKLISNFSK VSGYKINVQKSQAFLYTNNRQ TESQIMSELPFTIASKRIKHLGIQ LTRDVKDLFKENYKPLLNEIKE DTKKWKNIPCSWAGRISIMKM AILPKVIYRFNAIPIKLPMTFFTE LEKTTLKFIRNQKRAHIAKSILS QKNKAGGITLPDFKLYYKATV TKTAWYWYQNRDIDQCTRTQP \SEITPHIYNYLIF
4367	34735	A	4408	1	1947	MALRRLSHDVSGALLLANGES TGNSGGSSGSSPSGGATSGSSQ TSISGDVVEACCSVLSMVCADP VYKVYVAAL\QCMLLVTLEDPS SHFTRMRRRLM/AYADEVEIAE AIQLGVEDTLDGQQDSF\CRHL FPTTIWKPQRTVP/LECTIHLEKT GKGLCATKLSASSEDISERLASI SVGPSSSTTTTTTTEQPKPMVQ TKGRPHSQCLNSSPLSHHSQLM FPALSTPSSSTPSVPAGTATDVS KHRLQGFIPCRIPSASPQTQRKF SLQFHRNCPENKDSDKLSPVFT QSRPLPSSNIHRPKPSRPTPGNTS KQGDPSKNSMTLDLNSSSKCD DSFGCSSNSS/NCCYT\SDETVFT PVEEKCRLDVNTELNSSIEDLLE ASMPSSDTTVTFKSEVAVLSPE KAENDDTYKDDVNHNQKCKE KMEAEEEEALAIAMAMSASQD ALPIVPQLQVENGEDIIIIQQDM TFFRHIIPPIQWIYKKESANLLID STGQRLRIADFGAAARLASKGT GAGEFQGQLLGTIAFMAPEVLR GQQYGRSCDVWSVGCAIIEMA CAKPPWNAEKHSNHLALIFKKL LDFANTACDGDKESEVEDVET DSGNSPEDLRKEIMIGLQYQAEI PPYLGEYDGNEKDSPQPKKMT GVQNAKEVLST

SEQ ID NO:	SEQ ID NO: of peptide sequence	Met hod	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
4368	34736	A	4409	1	4485	
4369	34737	A	4410	2	927	IDHMIGHKASLNKFKKIEIISSTLSGHNGIKLEINSKRDLQNHANTRK\LNNLLLNEHWVKNEIKMEILKFFELNDHNDTTYQNLWDTAKATF\LLRGKFTALNAYIKKTERAQTDILRSHVKELEKQEQTKPKPSRRKEITKIREELNEMETNKKKIQKINETKSRFFEQINKIDRSLARLAKKRREKIQITSIRNKTGDTTTDTTEIQKIIQGYYEHLYAHKLENLEEMDKFLEKYNPPSLNQEELDTLNRTITSNKIEMVIKKLPTKKKSPGPNGFTAEFYQTFK\EELVPILSILVHKTEKEGTLP
4370	34738	A	4411	405	517	
4371	34739	A	4412	1	1197	MEISELNAKLRSQEKEKQNEIIKLQLEKLQHFQEEKNKEIAILRNTIRDLEQRLSVGKDSHLKRENEQLKISADLIKEKLKSHEQEYKNNIAKLVSEMKIKEEGYKKEISKLYQDMQRKGRIKVTCEWTCSERKTEGREPGPVREPTGRSQSAENEGSKTLAEINTKGTQSPAERINKIDRLLARLTNKRREKVQISSIRNKTGDIRTDTTEKQKFMQGYHEHLYMHKLENLKEMDKFLEIYSPPRLKREDIETLSRPITISDIEMKNLKIPPKLPELINKFSKVSRYKINVHKLVALLYANSDQTDNQIKNSTHFTIVAKK\YLGIYLTKDMKDLHKENSK/PLLKEIIDDTIKWKHIPCSWMSTTNIVKMTILPKTIYKFNAIIIKIPPSFFAERKKQS
4372	34740	A	4413	1	190	MIQRKRASIGAPCAWVRKKEEEEEEEEEEEEEEEEEEEEE\KKKKKKKKERTTWLWGNPLT
4373	34741	A	4414	303	429	
4374	34742	A	4415	123	252	
4375	34743	A	4416	1	156	
4376	34744	A	4417	3	351	EEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEEE\KEEEEEEEEEEEEGEEEELGRLHGGSGKVRGLGFTENQQGSTNRQHQREDNRKSKQKKINNTKPEATESLIVNGITITAPA
4377	34745	A	4418	1	192	
4378	34746	A	4419	3	259	
4379	34747	A	4420	1	279	
4380	34748	B	4421	1	708	
4381	34749	A	4422	3	269	

SEQ ID NO:	SEQ ID NO: of peptide sequence	Met hod	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
4382	34750	A	4423	1	322	MAGKQGRSEGASSWRLSSVLQLNSQYFLQGAQQCTFLAATAWKKRKEEEEEEEEEEEEEEEEEEEEEEEEEEEEE\KKKKKKKKKKKKKKKKKKKKKKKKKKKKKKKKKKKKKKKKKKKKKKKKKKKKENPFSCF
4383	34751	B	4424	327	674	
4384	34752	A	4425	494	960	TRFYDHALHLIHRKGSTTVRSPPPLYFIGESKASALLAISLRWSGRSQPRSSVNQIRKAWGFRPRKGTEE/DERSGCPSDALESDDPMAYIHFTAEGEVTFKSILFVPTSAPRGLFDEYGSKKSDYIKLYVRRVFITDDFHDMMPKYLNFVKGVV
4385	34753	A	4426	1	2539	VGGPRGWRCEDPNPGVGGGGGSCDRRGLETHRPHAMRALWVLGLCCVLLTFGSVRADDEVDVDGTVEEDLGKSREGSRTDDEVVQREEEAIQLDGLNASQIRELREKSEKFAFQAEVNRMMKLIINSLYKNKEIFLRELISNASDALDKIRLISLTDENALSGNEELTVKIKCDKEKNLLHVTDTGVGMTREELVKNLGTIAKSGTSEFLNKMTEAQEDGQSTSELIGQFGVGFYSAFLVADKVIVTSKHNNDTQHIWESDSNEFSVIADPRGNTLGRGTTITLVLKEEASDYLELDTIKNLVKKYSQFINFPIYVWSSKTETVEEPMEEEEAAKEEKEESDDEAAVEEEEEEKKPKT\KKVEKTVWDWELMNDIKPIWQRPSKEVEEDEYKAFYKSFSKESDDPMAYIHFTAEGEVTFK\SILFVPTSAPRG\LFD\DYGSKK\SDYIKLYV\RR\VFITD\DFHDMMPKYLNFVKGVVDSDDLPLNVSRETLQQHKLLKVIRKKLVP*NRWDMIKKI/SLDDKYNDTFW\KEFGYQHSSLVVIEGPLRIRTRLAKLLR\FQSSHHPTD\ITSLDQYVERMKEKQDKIYFMAGSSKKEAESSPFVERLLKKGYEVIYLTEPVDEYCIQALPEFDGKRFQNVAKEGVKFDESEKTKESREAVEKEFEPLLNWMKDKALKDKIEKAVVSQRLTESPCALVASQYGW

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4386	34754	A	4427	2	622	PARAALGILTSHQSGFLKTSTSKIT\STAWKN\KDITMQSTKQYACLHDLTNKGIGEEIDNEHPWTKPVSSENFT\SP\YVWMLDAEDLADIEDTVEWRHRNVESLCVMETASNFSCS\TSGCFSKDIVG\LRTS\ACWQQHCASPAFAYCG\HSFCCTGTALRTMSSLPESSAMW*KKPARTRLPRGKDLIYFGSEKSDQETGTLLLPVSS
4387	34755	A	4428	2	1421	QHCSQKDTAELLRGLSLWNHAEERQKFFKYSVDEKSDKEAVSEHSTGITHLPPEVMLSIFSYLNPQELCRCSQVSMKWSQLTKTGSLWKHLYPVHWARGDWYSGPATEL\DT\EPDDEWVKNR\KDESRAFHEWDEDADIDESEESAEESIAISIAQMEKRLLHGLIH\NVLPYVGTSVKTLVLAYSSAVSSKMVRQILELCPNLEHLDLTQTDISDSAFDSWSWLGCCQSLRHLDLSGCEKITDVALEKISRALGNSGHLHQSGFLKTSTSKITSTAWKNKDITMQSTKQYACLHDLTNKGIGEEIDNEHPWTKPVSSENFTSPYVWMLDAEDLADIEDTVEWRHRNVESLCVMETASNFSCSTSGCFNHRPWSQNEYEQLNYAKQLKERLEAFTRDFLPHMKEEEEVFQPMLMEYFTYEELKDIKKKVIAQHCSQKDTAELLRGLSLWNHAEERQKFFKYSVDEKSDKEAVS
4388	34756	B	4429	70	348	
4389	34757	A	4430	2	371	
4390	34758	A	4431	1	907	MGHRINIVCKIDAPCARQTRTFHPVVKTVEDCGRYPSVIEFGKYEIQTWYSSPYPQEYARNLAKEGKMGEREMSFVQQLQPMSGRCSLF\RELSSCTYLLNTQPP/AVSIHFLAVWIILLVDGNMSKIYCQNLCLLAKLFLDHKTLYYDVEPFLFYVLTKNDEKGCHLVGYFSKWTVLQGQWQVQGIAHFSRALTYLICFSFPQEKLCQQKYNVSCIMIMPQHQRQGFGRFLIDFISFPRLTIGASFTQLRKQSMSNST\EIPLLGDNGKSSPTFHWQSLTSSPNAHFSLEAQLSILGHLFQSP

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4391	34759	A	4432	1	3468	MGKKQNRKTGNSKNQSASPPP KERSSSPATEQSWMENDFDELR EEGFRLSNYSELPEDIQTKGKE VENFEKNLEECITRITNKRNFKP TKIKRDKEGHYIMVKGSIQQEE LTILNIYAPTGAPRFIKQVLSDR QRDLDFHTLIMGDFNTPLSTLD RSTRQKVNKDTQELNSALHQA DLIDIYRTLHSKSTEYRFFSAPH HTYSKIDHLLGSKAFLSKCKRT EIITNYLSDHSAIKLELRIKNLTQ NRSTTWKLNN
4392	34760	A	4433	3	1900	FNKCMTLKFRLKNFSRINKIDTP LARLIKKKREKNRIDTIKNDKG DITSNPTEIQSTIREYYKHLYTN KLENLEEMDKFLDTYTLPRLNQ EEVESLNRPITGSEIMAIINSLPT KKSPGPDGFTAKFYQRYKEELV PFLLKLFQSIEKEGILPNSFYEAS IILIPKPGRDTTKNENFRPISLMN IDAKILNKILANRIQQHIKKLIH HDQVGFIPGMQGWFNIRKSINV IQHISRTKDKNHMIISIDAEKAF DKIQQPFMLKTLNKLG\IKYLGI QLTRDVKDLFKERS/YEPLLNEI KEDTNKWKNIPCSWVGRINIVK MAILPKVIYRFNAIPIKLPMTFF TELEKTTLKFIWNQKRALIAKSI LSQKNKAGGITLPDFKLYYKAT VTKTAWYWYQNRDIDQWNRT EPSEITLHIYNYLIFDKPEKNKQ WGKDSLFNKWCWENWLAICR KLKLDPFLTPYTKINSRWIKDL NVRPKTIKTLEENLGITIQDIGM GKDYMSKTPKAMATKAKIDK WDLIKLKSFCTAKETTIRVNRQ PTKWEKIFATYSSDKGLISRIYN ELKQIYKKKTNNPIKKWVKDM NRHFSKEDIYAAKKHMKKCSP SLAIREMQIKTTMRYHLTPVRM AIIKKSGNN
4393	34761	A	4434	2	1932	

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4394	34762	A	4435	1	2571	MKAEIKMFFETNENKDTTYQNLWNTFKAMCRGKFIALNAHKRKQERSNTDTLTSQLKELKKQEQTHSKPSRRQEITKIRAEMKEIETQKTLQKIKESRTWFFEKINKIDRLLARLTKKKREKNQIDAIKNDKGDITTDPTEIQTTIREYYKHLYANKLENLEEMDKFLDTYTLPRLNQEEVESLNRPITGSEIEAIINSLPT/KKCPGPDGFTAEFYRRKRG\ILPNSFYEASIILIPKPGTDTTKKENFRPISLMNIDVKILNKILANRIQQHIKKLIHHDQVGFIPGMQGWFNIRKSINIIQHINRAKDKNHMIISIDAEKAFDKIQQCFMLKTLNKLGIDGTYLKIIRAIYDKPTANIILNGQKLEVFPLKTGTRQGCPLSPLLFNIVLEVLARAIRQEKEIKGIQLGNEEVKLSLFADDMIVYLENPIISAPNLLKLINNFSKGSAYKIKVQKSQAFLYTNNRQTESQIMSELPFTIASKRIKYLGIQLTRDVKDLFKENYKPLLKEIKEDTNKWKNIPCSWVGRINIMKMAILPKVIYRFNAILIKLPMTFFTELEKSTLKFIWNQKRARIAKSILSQKNKAGGITLPDFKLYYKATVTKTAWYWYQNRDIDQWNGTEPSEIMPHIYNYLIFDKPEKNKQWGKDSLFNKWCWENWLAICRKLKLDPFLTPYTKINSRWIKDLHVRPKTIKTLENLGNTIQDIGMGKDFMSK

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4395	34763	A	4436	1	1965	MTLESEQTFVYAVTATQTGAK EGTRMSKSNVAGQQGDSGEKA LQKTYQKILREKESALEAKYQA MERAATFEHDRDKVKRQFKIF RETKENEIQDLLRAKRELESKL QRLQAQGIQVFDPGESDSDDNC TDVTAAGTQCEYWTGGALGSE PSIGSMIQLQQSFRGPEFAHSSID VEGPFANVNRDDWDIAVASLL QVTPLFSHSLWSNTVRCYLIYT DETQPEMDLFLKDYSPKLKRM CETMGYFFHAVYFPIDVENQYL TVRKWEIEKSSLVILFIHLTLPRI KYLGIQLTRDVKDLFKENYKPL LNEIKEDTNKWKNILCSWTGR NNVMKMATLPKVIYRFNAIPIK LPMTFFTELEKTTLKFIWNQKR AHIAKTILSEKNKAGGIMLPDF KLYFKATVTKAAWYWCQNRD IDQWNRTEASEITPHIYNHLIFD KPDKNKKWGKDSLFNKWCWE NWLAICRKLKLDPFLTPYTKIN SRWIKDLNVRPKTIKTLEENLG NAIQDIGMGKDFMTKTPKAMA TKAKIDKWDLIKLKSFCMAKET PIGVNRQLTEWEKIFAIYPSDKG LISRIYKELKQTYKKKTNNPIEK LAKEMNRHLSKEDIYAANRHK KKCSSSLVIREMQIKTT/MRYHL TPVRMAIIKKSGNNRCWRGCG
4396	34764	A	4437	300	476	PDLSLWLPLTFFPSFQLW*I*QL CVLELLFSRSIFVAFSVFPEFES WPALLGWGSSPG

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4397	34765	A	4438	413	1689	QKLYKPERIKYLGIQLTRDVKD LFKENY/KLNEIKEDTNKRKNIP CSWVGRINILKMAILQKVIYRF NAIPIELPITFFTKLEKTTLRFIW NKKRVHIAKSIPSKKNKAGGIM LPDFKLYYKATITKTAWYLYQ NRDIDQWNRTEALGITPHIYNH LIFDKPDKNKQRGKDSLFNKW CWENWLVICRKLKLDAFLTPY TKINSRWIKDLNIRPKTIKTLEE NLGNTIQGIGMGKDFMTKTPK AMATKAKIDKRDLIKLKSFCTA KETNIRVNRQPIEWEKIFAIYRS DKGLISRIYKELKQIYKKKTNN SIKKWAKDMNRHFSKEDIYAA NRHEKKWSPSLVTREMQIKTIM RYHLTPVRIMTIKMSGNNRCW RGYGEIGMLLHCWWECKLVQ ALWKTVWRFLKDLELEIPFDPV IPLLGIYPKDYT
4398	34766	A	4439	3	2404	
4399	34767	A	4440	1	1572	MLVSFVSLGSLCLQPGSQTLLE KNRTVKPHVSFTLLPALSHVSE KNEAESMNSLIPPPPNLHTPAQ APFPLPTKEQDRSSSPATEQSW TENDFDELTEVGFRRSVITNSSK LKEDVRTHCKEAKNLEKRLHE WLTRINSVEKTLNDLKLKSMA RELHDTCTSFNSRFDQVEERVS AIEDQTNEINNGENGTKLENTL QDIIQENFPNLARQANIQIQEIRR TPQRYSSRKATPRHIIVRFTKVE MKEKVLRAAREKVLEVLARAI SQEKEIKCTQLGKEEVKLSLFA DDMIVCLENPVVSDHNVLKLIS NFSKVSVYKINVQKSHAFLYTN NRQTESQIMSELPFTITTKRIKY LGIQLTRAVKDFFKEKYKPLLN EIKKDTNKWKNIPCSCIGRINIM KMAIVPKVIYGFNAIPIKLPRTF FTELEKTTLKFIWKKKGAKTILS IKNKAGGIMLPDFKLYYKATVT KIAWYWYQNRYINQRNRTETS EITSHIYNHL/IFDKPDKNKKWG KDSLFNKWCWENWL
4400	34768	B	4441	1	1558	

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4401	34769	A	4442	837	4329	TWKGTTDRSTRQKVNKDTQELNSALHQADLIDIYRTLHPKSTEYTFF/LAPHHTYSKIDHIVGSKALLSKCKRTEIITNYLSDHSAIKLELRIKNFTQSRSTTWKLNNLLLNDYWVHNEMNAEIKMFFETNENKDTTYQNLWDAFKAVCRGKFIALNAHKRKQERSKIDTLTSQLKELEKQEQTHSKASRRQEITKIRAELKEIETQKTLQKINESRSWFFERITKSDRPLARLIKKKREKNQIDTIKNDKGDIT
4402	34770	A	4443	1	816	MRRDYPVKAFTSRKREQHVQKVPSKKSRQVQRTERRFLETTPDLLYQKEKDLLLISSSKKQPRPGIERHYMMTQGSIHQEDVAILK/VYTSNKRASKYIQQ/TLLEIKGKI/AHPQIVGDFNTPTSTIDRTIRQQISIEFYDTIKQWDLTDTCRTGHPITEYIFCSGAHLTFTKINHIQGPKRILKRFKRIEIIECVLVLKGCQAKNRKKEEDLQTYWMLNIYGPHYRSGSYAAIHRQETICSGQLSQALRDRFAMNAKLLLSLAAHLWVIKLDFM
4403	34771	A	4444	87	307	
4404	34772	A	4445	1	534	MEESRGAKPPPALLPGDATLPPGSLGSARHPPEP/RPVPGP/PPHQTCPGPSACSSRRPEPRSSPGSPARAPPAPPPPAAPAPRCEPPLWLLLRVPCPGRSGWSWMTT*I/SERPVQKRARSGPQPRLPPCLLPLSPPTAPDRATAVAT\PPVLGPMSSWSPRRAGGPTRPCTALQALSIPA
4405	34773	A	4446	164	660	YPSGRRLREPADVADAWDGMEESRGAKPPPALLPGDATLPP\APSGQLGTRPSPPSSRPSPHQTCPGPSACSSRRPEPRSSPGSPARAPPAPPPPAAPAPRA/SPRRPLPAPRSASVPAFSAPPSQWPEVGPSPCALRRAMPRGPGPPPEPRLVAEPGEDAAPTAGR
4406	34774	A	4447	1	417	

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4407	34775	A	4448	1	1802	MSYPADDYESEAAYDPYAYPSDYDMHTGDPKQDLAYERQYEQQTYQVIPEVIKNFIQYFHKTVSDLIDQKVYELQASRVSSDVIDQKVYEIQDIYENSWTKLTERFFKNTPWPEAEAIAPQVGNDAVFLILYKELYYRHIYAKVSGGPSLEQRFESYYNYCNLFNYILNADGPAPLELPNQWLWDIIDEFIYQFQSFSQYRCKTAKKSEEEIDFLRSNPKIWNVHSVLNVLHSLVDKSNINRQLEVYTSGGDPESVAGEYGRHSLYKMLGYFSLVGLLRLHSLLGDYYQAIKVLENIELNKKSMYSRVPECQVTTYYYVGFAYLMMRRYQDAIRVFANILLYIQRTKSMFQRTTYKYEMINKQNEQMHALLAIALTMYPMRIDESIHLQLREKYG\DKMLRMQKGDPQVYEELFSYSCPKFL\SPVVPNYDNVHPNYHKE\PFLQ\QLKGVF**SSSQQAQLS/TPIRSFLKLYT\TMP\VAKLAGFPGPSQSQEF\RIPGFFVFKQQDERTSVWTQRVFSAPGW*NFSQASEVDF\YI\DKDMI\HIADTKVA\RRYG\DFFIRQI\HKF\EELNRTLKEGWGQRPWMIFHTHFREPGFECIIGQGSVFC

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4408	34776	A	4449	1	1722	MNIKAKILNKILANRIQQHIKKLIHHDHVSFIPRMQGWFNIHKPINVIHHINRTNDKNHMIISIDAEKAFDKIQHPFTLKTLNKLDDMTVYLENPIVSAQNLLKLISNFSKVSGYKINVQKSQAFLYTNNRQTESQIMSELPFTIASKRIKYLGIQLTRDVKDLFKENYKPLLKEIKEDTNKWKNIPCSWVGRINVVKMAILPKVIYRFNAIPIKLPMTFFTELEKTTLKFIWNQKRARIAKSI\LSQKNKAGGITLPDFKLYYKATVTKTAWYWYQNRDIDQWNRTE\PSEIMPHIYNHLTFDKPDKNKQWGKDSLFNKWCWENWLAICRKLKLDPFLTPYTKINSRWIKDLNVRPKTIKTLEENLGNTVQDIGMCKDFMTKTPKAMATKAKIDKWDLIKLKSFCTSKETIIRVNRQPTEWEKMFAIYPSDEGLISRICKE/LFKQIYKKKNHPIKKWAKDMNRHFSKEDIYVANKHMKKSLSSLVIREMQIKTTMRHHLTPVRMTIIKKSGNNRFWRGCGETGMLLHCWWECKLVQPL*KIVW*FLKDLESEIPSDSAIPLGGIHPKAYKSFYY
4409	34777	A	4450	1050	1147	PGEWHGQGSPRCWR*PLPQRCGHLLSCRWRTP
4410	34778	A	4451	1	614	MEELVDEGLVKALGVSNFSHFQIEKLLNKPGLKYKPVTNQNSLGTMQNRAGFPRDEDCLLLQVECHPYLTQEKLIQYCHSKGITVTAYSPLGSPDRPWAKPEDPSLLEDPKIKEIAAKHKKTAAQVLIRFHIQRNVIVIPKSVTPARIVENIQNTEHYKYCGLCVGPNLEKNLYPVDRM/WKNSCGQFVL*ISSHLEDYPFNAEY
4411	34779	A	4452	2	240	WMELESLSHFQIEKLLN/KPGLKYKPVTNQVNSIQFKGSILEEGIVNMGDDSSMHVSAPEDPPVGQDVEAEDSDTDDPDPV
4412	34780	A	4453	1	1019	
4413	34781	A	4454	1	2028	

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4414	34782	A	4455	3	1045	DFTSENFSAAWYLIENHSNTSFEQLKMAVTNLKRQANKKSEGSLAYVKGGLSTFLEAQDALSAIHQKLEADGTEKVEGSMTQKLENVLNRASNTADTLFQ/EKVLGRKDKADST\RNALNVL\QRFKFLFNLPLNIERNIQKGDYDVVINDYEK\AKSLFG\KTEVQVF\KKYYAEV\EPRVEALRELLL\DKLLETPSTLHDQKRYIRYLSDLHASGDPAWQCIGAQHKWILQLMHSCKEGYVKDLKGKDFSSNVFQFSGSALRRVPDTVRVLDSQFSRSALRSVPDTVQVLDSQFSGSALRRVPDTVRVLDGQFSRSALRSVPDTVRVLDKCHCSPAKVVMNAVTIFTG
4415	34783	A	4456	1	440	MQRNLARAFSPGIKKIKMMCLGNSEKDWPKFRGVGEDAGLLAARECGALLVIRHLINAVRAIVPNKSNNEIILVLQHFDNCVDK\TVQAFMEGSASEVLKEWTVTGKKKLLLQGEEELARLPFITGGSGSCYSSSTLAVEEECRVLA
4416	34784	A	4457	1	276	MEDEMEGLTEAGFRRWVTTNSAELKEHVLTQCKEAKNLDKRLEELLSRITSLERDISDQME/RELCEAYTSINSQINQAEERISEFEDHLAEI
4417	34785	A	4458	3	361	EMVHRKKKAVHRTATADDKKLQFSLKKLEVNNVSGIEEVNMFTNQGTVIHFN\AEMPANSFTITGHAETKQLMEMLPSILNQLGAHCLTSLRRLAEALPKQSVNGKAPLATGEDDDEVPA
4418	34786	A	4459	1	475	
4419	34787	A	4460	57	820	EDGSGGGKFPEGARQGGTGQRRRRKAMRRTGAPAQADSRGRGRARGGCPGGEATLSQPPPRGGTRGQEPQMKETIMNQEKTRHTCRAQ\VRIGGKGTARRKKKVVHRGAAS/ADDKKLQF\SLKK\LGVNNISGIE\EVNM\FTN\QGTSGSTFNNP*KFQGISWPANTFHHLQGHAEDKGS*QEMLAQHLKPSLGADSLTSLRRLAEALPKQSVDGKAPLATGEDDDDE\VPDLV\ENF**RLPRNEANLNLSQLLKIKP
4420	34788	A	4461	1	1527	

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4421	34789	A	4462	8	327	LIWQLTFTKTIKS/CEEYGKIVSTKAILDKNTNQCKGMCKGIRTLKSCLCYLINGSSIVEVQKRLAYAGTLEPSLVHQVYSELSYYKLPGTQVVRIIAEVLRMQDSSE
4422	34790	A	4463	2	573	WMEGREKWRGRRKDGRKEGRKEGRKERRREREKGRERK/GKERKGKERKGKERKGKERKGRERKGTEGKGTEGKGKERKGKEGKGKERKGKERKGKERKGKEGKGKEQKGKERKGKERKGKERKGKERKGKERKGKEEKGRERKGKEGKGRERKGKEGGKEEGRKERRKEGRKEGKKFSNNGMVEEMQ
4423	34791	B	4464	1	1344	
4424	34792	A	4465	3	373	
4425	34793	A	4466	1	3864	MQWEEAEKDPSGSCVFQRPPVALVFPLHSKWTLVNSPPSSGDPYVPGRPAQSGQLSLSPAPPYVLPGPGKIKQAGNNPSLTSIYRSEVFCAHRHLHPPQLVCARGHIGSAHLSVDRGSLIWEVLESTVWARTNEWSPVTRTVLISALASTHIPQPCESRPPVPPEYEVTVLRSQGTAQLPPWSSSTSWRLTDPSCPKHAAWLTDLASSKGPAAGGTGSFSQPGTLTSTRTNPLKKEKSPEDLKQIKIDLGKFSDN
4426	34794	A	4467	3	415	
4427	34795	A	4468	396	676	LCFPYAERPDLQFLC*DLCARSPYLLQAQKYLQEF*AIPHLDQQTEPPDPSVSFYLLDCTLNCTAQHKTC*KKSIGL*EQNQQTLSSIPYSHT
4428	34796	A	4469	1	858	MEWEDNLPLELGRTVAKLLSDHSQTPLGIQMFLLFSLSLRKSPLVCLSYLFNFRFTLESEVQHLSGAITLTAWPKIPFLGIREAKSPRSENTRLATILEAGHRHLGTSVSKDHPVTFWRPRRDLQSDLKQIKIDLGKFSDNPDGYIDVLQELGQSFDLTWRDIMLLLNQTLTPNERSATITAAREFGDLWYISQVVAAVAGLVSEAVKIIQG\LTVWT/SHDVNGILTAKGDLWLSDNHLLKYQALLLEGPVLRLRTCATLNPATFLPDNEEKIEHNCQQVIAQTYA
4429	34797	A	4470	918	1939	

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4430	34798	A	4471	3	2693	PQVCLTIESQEVNCLLDAGAAFSVLLSCPGQLSSRSVTIRGVLGQPVTRYFFQPLSCDWGALPFSHAFLIMPESLTPLLEREILVKAGAIIHLNIGEGTPICRLLFEEGISPEVWATEGQYGQAKNAHFVQVKLKDSTSFPYQRQYPLRPEAQQRLQKIVKDLKAQGLVKPYSSPCNTPILGVQKPKRQWRLVQDLRIINEAVFPLYPAIPSPYTLLSQIPEEAEWFTVLDLKDAFFCIPVHPDSQFLFAFEDPSNPTSQLTWTVLPQGFRDSPHLFGQALAQDLSQFSYLDTPVLQCMDDLLLAARSETLCHQATQALLNFLTTCGYKVSKPKAQLCSQQVKCLGLKLSKVTRALSEERIQPILAYPYPKTLKQLRGFLGITGFCRIWIPRYGKIARPLYTLIKETQKANTHLVRWTPEAEAAFHALKKALMQAPVLSLLTGQDFSSYVTKNKQTKKKK\T*IALRVLALV*GTSLQPVAYLSKKTDVVAKGWPHCLWVMAAIAVLISKAVKMIQ*RDLTVWTSHDVNGILTAKGDLWLSDNHLLKYQALLLEGPMLRLCTCAALNLDTFLPHNEEKIEHNCQQVIAQTYATRGDHLEVPLTDPNPNLYTDGRSFVEKGLQKVGYAVVSDNGILESNPLTPGTSAQLAELIALTWALELGEGKRVNIYTDSKYAYLVLHAHAVIWREREFLTSEGTPIKHQ
4431	34799	C	4472	11	1639	
4432	34800	A	4473	95	2539	
4433	34801	A	4474	345	768	PRGARSTRCLPVERR\CDGLQDCGDGSDEAGCPDLACGRRLGSFYGSFASPDLFGAARGPSDIHCTWLVDTQDSRRVLLQLELRLGYDDYVQVYEGLGERGDRLLQTLSYRSNHRPVSLEAAQGRLTVAYHARARSHPLMNE
4434	34802	A	4475	47	563	RLRFAVFTGAFHALSFLLSFVVLCCTYLKGLKVARFHCKRIDV/MHHADARAAGGPAPQCAGTLS\EEQKRRRQRATKKISTFIGTFLVCFAPYVITRLVELFSTVPIGSHWGVLSKCLAYSKAASDPFVYSLLRHQYRKSCKEILNRLLHRRSIHSSGLTGDSHSQNILPVSE

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4435	34803	A	4476	1	332	ERGRQEMSAKLRPPAEPPCVPARISP*RPS*RQ*MERRCPPWRCSPMPC/CFFREHALQVRCGPTSADCGRDPLFSPHPKPLPHPVPDIGWVATAGAQRSSSPVPSSLFVW
4436	34804	A	4477	297	943	TGSWGGGGADQLRPALTTALMPPDNRFGENTPAAPANGHCAP\EPDITLVQDHSELPIGAAATMAHEIGHSLGLSHDPDGCCVEAAAESGGCVMAAAT/GVRGHPFPRVFS/SCSRRQLRAFFRKGGGACLSNAPD/TRTPGAAALCGNGFVEAGEECYCVS\GQECRDLCCFAHNCSLRPGAQCAHGDCCVRCLVR/CMEGSGSHQLPRLVPGGDSAEILM
4437	34805	A	4478	1	836	MGPLTFRDVKIEFSLEEWQCLDTAPGNLYRDVMLENYRNLVFLVMCSHFAQDVWPEHSIKDSFQKVILRTYGKYGHENLQLRKDHKSVDACKVYKGGYNGLNQCLTTTDSKIFQCDKYVKVFHKFPNVNRNKIRHTGKKPFKCKNRGKSFCMLSQLTQHKKIHTREYSYKCEECGKAFNWSSTLTKHKIIHTGEKPYKCEECGKAFNRSSNLTKHKIIHTGEKPYKCEECG\KAFNRSSTLTKHKRIHTEEKPYKCEECGKAFNQFSILNKHKRIHMGR
4438	34806	A	4479	1	588	MLGKVQQQEQTIAKDLVVTKYKMCGGT/DIANRVLRSLVEASSS\GGQDYILKEGDLVKIDLGVHVDGFIANVTHTFVVDVAQGTQVTGRKGDVIKAAQLCVEAALCLVKPGNQNIQVREAWSKVALSFNCMPIEGMLSHQLKQHVIDGEKNIIQNPTDQQKKDHEKAEFEVHEVYAADVLVSSGEGKAKDAG
4439	34807	A	4480	85	561	LSHCLPLQTTEVGGFGNLLGYWIACSIGCVLSTGMLSHQLKQHVIDGEKTIIQNPTDQQKKDHEKAEFEVHEVYAVDVLVSSGEGKVRRVPELAKRGD*ECSPDQMLLKLLFQAKDAGQRTTIYKRDPSKQYGLKMKTSRAFFSEVERRFDAMPFTLRY

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4440	34808	A	4481	1	1408	GTSAPQPARSQLLALACLPAPL LARAFARPLLEDRGDSDHSLW LGRETEAAAAQGKRGCSGGSR KMSGEDEQQEQTIVD/DSLVVT KYKMGGDIANRVLRSLVEASSS GVSVLSLCEKGDAMIMEETGKI FKKEKEMKKGIAFPTSIS\VNNC VCHFSP/L*KSDQDYILKEGDLV KIDLGVH\VDGFIANVAHTFVV DVAQGTQVTGRK\ADVIKAAH L\CAEAA\LRLVKPGNQNTQVT\ EAWNKVAHSF\NCTPI\EGMLSH SLKQHVIDGEKP*FQNPTDKQK\ RAHEKADFEVH\DVYAVEGLV KPQERARPKDAGQRTTIYKRDP SKQYGLKMKTSRAFFSEVERRF DAMPFTLRAFEDEKKARMGV\ VECAKHEL/VWQPFNVLYSGRE GDFVCPVLNFTVL\LMPNGPML ITSGPFEPDLYKSQMEVQ\DAEL KALLQSSASRKTQKKKKKKAS KTAENATSGETLEENEAGD
4441	34809	A	4482	3	190	
4442	34810	B	4483	1	588	
4443	34811	A	4484	1	1312	MSSKGSVVLAYSGGLDTSCILV WLKEQGYDVIAYLANIGQKED FEEARKKALKLGAKKVFIEDVS REFVEEFIWPAIQSSALYEDRYL LGTFF\ARPCIARKQVEI\AQREG AKYVSHGATGKGNDQVRFELS CYSLAP\QIKVIAPWRMPEFYNR FKGRNDLMEYAK\QHGIPIPVTP KNPWSMDENLMHISYEAGILE NPKNQAPPGLYTKTQDPAKAP NTPDILEIEF\KKGVPVEGGPTF KDG\TTHQTFL\ELF\MYLNEVA GKHGVGPYLTSWENRFHWELK SRGILRRPQAG\TILYHAHLDIE AFTMGGDRAQIPNQGLGFEFVE LGVYRFSGTAPECELVGPCLRQ SPQERVEGKSAGVPSLKGPRCT SLGPEVPHCSLYNE\ELVKHGT CQGDYE\PN*LPPGFIQTSISLKA EGNYHRLPRAKVTAQIRPRVQ
4444	34812	B	4485	47	482	

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4445	34813	A	4486	2328	3435	KTTTLEDNLGNTIQDIGPGKDF MMKIPKANATKIKIDEWDLIKL KSFCTAKATTKRVNKHDESLRS HYE*WGMLTDCVVMRDPNTK RSRGCGFVTYATVEEVDAATN ARPHKVDGKVVEPKRTVSRED SQRPGAHLTVKKIFVGGIKEDT GGFAFVTFDDHDSVDKIVIPKY HTVNGHNCEVRKALSKQEMAS ASSSQRGRSGRGGGFGGNENFG CGGNFSGHGGFGGSHDGGGYG GSGDGYNGFGNDGGYPGGGPG YSGGSRGYGSGGQGCGNQDSG YGRSGSYDSCNKGGRGGFGSG SGSNFGGGGSYNDFGNYNNQY SNFGPMKGGNF/GGRRSGP*GD GGQYFAKPPNHSGYGGSSSSSS
4446	34814	A	4487	1	762	
4447	34815	A	4488	3	333	
4448	34816	A	4489	1	1676	MRDPNTKRSRGFGFVTYATVE EVDAAMNTTPHKVDGRVVEPK RAVSREDSQRPGAHLTVKKIFV GGIKEDTEEHHLRDYFEQYGKI EVIEIMTDRGSGKKRGFAFVTF DDHDSVDKIVIQKYHTVKGHN CEVRKALPKQEMASASSSQRG RRGSGNFGGGRGDGFGGNDNF GRGGNFSGRGGFGGSCGGGGY GGSGDGYNGFGNDGSNF*G\GG SYNDSGNYNNQSSKFEPMKGG NFGGRSSGPYGGGGQYFAKPQ NQAARCVAARWLFRTEARLVF LQKFPPWAVVEVVTVIVAAPA AATATTRDGGGCSRNCNIPEVF PELLGCPNRRGPPGGVREKQQQ TNSKSTRRQEITKTIAELKEIETR KTLQKINESRSWFYEKINKVDR LLDRLIKKKREKSQIDAIKNDIG DIVTDPAEIQTTIKEYYKRLYAN ELENLEEMDKFLATYSLHSLNQ EEVESLNKPVTSSEVEAVTNSL PTKKSPGPDGFTVLLEVLAPAIR QEKEIKHIPIGREEVKLSLFADD VIVYLENPIVSAQNLLKLISNFS

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4449	34817	A	4490	1	1445	MKCLKFINHKEILEASERKQAESLDFPFKKLRWHLCEGWIEEERDESRKSETIFKDLFKVPVLKETIYYKFYGPPVYQIETVYFMALSPPKSKQFDKTKQNNNNKKTHQFVIVFFKTDEHLSARGRRRRSIVKVSLLPAVIGLKSKFLKKPDQLRKLF\IGGLSFETTDESLRSHFEQWGTLTDCVVMRDPNTKRSRGFGFVTYAT\VEEVDAAMNARPHKVD\GRVV\EPKRAVSREDSQRPGAHI/TLVKKIFVGGIKEDTEEHHLRDDYFEEIILNSMEKIEV\IEIMT\DRGSGKKRGFAF\VTFDDHDSVDKIVI\QKYHT/VGNGHNCEV\RKALSKQEDG*VLHPAQRG\RSGSGKLLVVGRGRWFSVGMDNFG\RGGNFSWSVVAFGGT\RG\GGGYGWQWGMAYNGFGNDG\SNFGGGG\SYNDFG\NYNNQ\SSNFGPMKGGNFG\GRSSGPYG\GGGQYF\AKPR\NQGGYGGSSSS\
4450	34818	A	4491	134	612	TVLNSMSVILAISTLLKIITGELLQSFGDGLLWNLVIGIRGIDGLSPKVRKVLQLLRLRQIFN/GTFVKLIKVTVNMLRTVEPYIAWGYPNLKSVNELIYKHGYGKISKKRIALTDNVLIARSLGKYGIICMEDLIYEIYTVGKRFKEANNFLWPFKL
4451	34819	A	4492	1	1983	
4452	34820	A	4493	1	1527	
4453	34821	B	4494	1	2211	
4454	34822	A	4495	1	2478	
4455	34823	A	4496	2	1544	
4456	34824	B	4497	1	2151	
4457	34825	A	4498	1	744	
4458	34826	B	4499	1	2172	

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4459	34827	A	4500	1	2535	MKSGHPEKEQDNSDVQETREITIRGLLCTALMRHSTGAIAYLGVLSGSASLKLAGVPLRCCEGDKDAGHPLETQTALCERGRGARSLVGNTIMTSQPVPNETIIVLPSNVINFSQAEKPEPTNQGQDSLKKHLHAEIKVIGVNLIQNVLERGWGKCQEMIYVLGLDICRPFFVSRVSEEGRMGQRGEEDANSLDFPPASLLCLICQEQGVNGESCSPVGMYHREIVPVYEVLSVITGLQIQVFSGKEADSVIKRSIGWGPFFKPRTKDKNHMIISIDAEKAFDKIQQHFMLKTLSKLGIDGTYLKIIRAIYDKPTANIILNGQKLEAFPLKTGTRQGCPLSPLLFNIVLEVLARAIRQEKEIKGIQLGKEEVKLSLFADDMIVYLENPIVSDQNLLKLISNFSKVSGYKINVQKSQAFLYTNNRQTESQIMSELPFTIASKRIKYLGIQLTRDVKDLFKENYKPLLNEIKEDTNKWKNIPCSWVGRINIVKMAILPKVIYRFNAIPIKLPMTFFTELEKTTLKFIWYQKRARITKSILSQRNKAGDITLPDFKLYYKATVNKTAWYWHQNRHIDQWNRTKPSEITLHIYNYLFFDNPDKNKKWGKDSLFNKWCWENWLAICRKLKLDPFLTPYTKINSRWIKDLNIRPKTIKTLEENLGITIQDIGMGKYFMTKTPKAMATKAKIDKWDLIKLKSFCTGKETTIRVNRQPT
4460	34828	B	4501	1	1785	
4461	34829	A	4502	1	1415	
4462	34830	B	4503	1	3262	
4463	34831	A	4504	1	278	

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4464	34832	A	4505	3	2528	ENKDTTYQNLWDAFKA\VCRG KFIALNAHKRKQEKSKIDTLTS QLKELEKQEQTHSKASRRQEIT KIRAELKEIDTQKTLQKINESRS WFFERINKIDRPLARLIKKKREK NQTDTIKNCKGDITTDPTEIQTT IREYYKHLYANKLENLEEMDK FLNTYTLPRLNQEEVESLNRPIT GAEIVAIISSLPT/K/KSPGPDGFT AEFYQRYKEE/LEKEGILPNSFY EASIILIPKPGRDATKKENFRPIS LMNIDAKILNKILAKRIQQHIKK LIHHDQVGFIPGMQGWFNIRKS INVIQHINRTKDKNHMIISIDAE KAFDKIQQRFLLKTLNKLGIDG TYFKIIRAIYDKPTANIILNGQKL EAFPLKTGTRQGCPLSPLLFNIV LEVLARAIRQEKEIKGIQLGKEE VKLSLFADDMIVYLENPIVSAQ NLLKLISNFSKVSGYKINVQKS QAFLYTNNTQTESQIMSELPFTI ASKRIKYLGIQLTRDVKDLFKE NYKPLLKEIKDDTNKWKNIPCS WVGRINIVKMAILPKLPMTFFT ELEK\TTLKFIWNQKRACIAKSI LSQKNKAGGITLPDFKLYYKAT VTKTAWYWYQNRDIDQWNRT EPSEIMPPIYNYLIFDKPEKNKQ WGKDSLFNKWCWENWLAICR KLKLDPFLTPYTKINSRWIKDL NVRPKTIKTLEENLGITIQDIGL GKDFMSKTPKAMATKAKIDK
4465	34833	B	4506	1	5401	
4466	34834	A	4507	1	5271	MNIDAKILNKILPNQIQQHIKKL IHHDQVGFIPGMQGWFNIRKSI NVIQHINRAKDKNHMIILIDAEK SFDKIQQPFMLKTLNKLGIDGT YFKIIRAIYDKPTANIILNGQKLE VFTLKTGTRQGCPLSPLLFNIVL EVLARAIRQEKEIKGIQLGKEEV KLSLFADDMIVYLENPIVSAQN LLKQISNFSKISGYKINVQKSQA FLYTNNRQTESQIMSEIPFTIAL KRIKYLGIQLTRDVKDLFKENY
4467	34835	B	4508	924	3423	
4468	34836	A	4509	525	673	RDSWGTCPVSGAGKVDWPPSS *HHR*HQQWCCGMPHQLSTKE NISIKDHLTKEKRKGGAV*RII

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4469	34837	A	4510	25	1766	GTCQFAAMNVVFAVKQYISKMIEDSGPGMKVLLMDKETTGIVSMVYTQSEILQKEVYLFERIDSQNREIMKHLKAICFLRPTKENVDYIIQELRRPKYTIYFIYFSNVI\SKSDVEVIGLKLIEQEVVAEVQEFYGDYIAVNPHLFSLNILGCCQGRNWDPAQLSRTTQGLTALLLSLKKCPMIRYQLSSEAAKRLAECVKQVITKEYELFEFRRTEVPPLLLILDRLDDAITPLLNQWTYQAMVHELLGINNNRIDLSRVPGISKDLREVVLSAENDEFYANNMYLNFAEIGSNIKNLMEDFQKKKPKEQQKLESIGS\MKA\FVENYPQFKKMSGTVSKHVTVVGELSRLVSERNLLEVSEVEQELACQNDHSSALQNIKRLLQNPKVTEFDAARL\VMLYALHYERHSSNSLPGLMMDLRNKGVSEKYRKLVSAVVEYGGKRVRGSDLFSPKDAVAITKQFLKGLKGVGNV\YTQLQPF\LH\ETLDHLIKGRLKENLYPYLGPSTLRDRPQDIIVFVIGGATYEEALTVYNLNRTTPGVRIVLGGTTVHNTKSFLEEVLASGLHSRSKES
4470	34838	A	4511	1	1335	MAPVTMMGYRSGKMGILADVQLQVGPPGPWLHLVVIAPVPECITGIGIFSSWGSPDVGPLLYDIRAIMWGSLAPAENTWILGNNHRRFLAQLKPRVIMQDFSNVISKSDVKSLAEADEQEVVAEVQQVITKEYELFEFRRTEVPPLLLILDRCDDAITPLLNQWTYQAMVHELLGINNNRIDLSRVPGISKDLREV\VSSAEIDEFYANNMYLNFAEIGSNIKNLMEDFQKKKPKEQQKLESIADMKAFVENYPQFKKMSG\TVSK\HVTVVG\ELSRL\VSERNLAGRFSEVEARNWAC\QNDHS\SALQNIKRLLQNPKVTEFDAARLVML\YA\LHYERHSSNSLP\GL\MMDLRN\KGVFWRKYSKARVLAVVEYGGKRVRGSDLFSPKDAVAITKQFLKGLKQQEIVNCVLAAANVYIKQLPLSIQPSASLNGCISLEKKPLVSTQRN
4471	34839	A	4512	1	816	
4472	34840	A	4513	26	257	
4473	34841	A	4514	56	236	

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4474	34842	A	4515	170	373	HSPRGSTASF/CEVSETKNPPIPDTPATREAEGLRSRLAVYSTRDSPCVACSGSYTQAQGSLGRKFQDP
4475	34843	A	4516	262	358	
4476	34844	A	4517	2298	2556	NHKNPRRKPRQYHSGHRHGQGLHD*NTKSNGTKSNGNKSQN*Q\WDLINLKSFCTAKETTIRVNRQPTEWEKIFTIYPSDKGLISRI
4477	34845	A	4518	801	944	DQEPTNSRHILATQMGPSPITKQSNPGV**KECGFSCSPRVWRYLVS
4478	34846	B	4519	85	660	
4479	34847	A	4520	693	827	
4480	34848	A	4521	272	339	
4481	34849	C	4522	532	2754	
4482	34850	B	4523	1	519	
4483	34851	B	4524	266	935	
4484	34852	A	4525	1	1584	
4485	34853	A	4526	1	723	GALPNGDRGRRKSRFALYKRPKANGVKPSTVHVISTPQASKAISCKGQHSISYTLSRNQTVVVEYTHDKDTDMFQVGRSTESPIDFVVTDTISGSQNTDEAQITQSTISRFACRIVCDRNEPYTARIFAAGFDSSKNIFLGEKAAKWKNPDGHMDGLTTNGVLVMHPRGGFTEESQPGVWREISVCGDVYTLRETRSAQQRGKLGLQTGDMAENT/TVHALPSNCMVWRRSQTRQQIS
4486	34854	A	4527	1	335	
4487	34855	A	4528	328	871	DCGGGRARTAIFAGAARAADNKKCAGARRALGRARGCSATARPRRRRRRPRGLAPPRPARPPPGGMSYKPNLAAHMPAAALNAAGSVHSPSTSMATSSQYRQLLSDYGPPSLGYTQGTGNSQVPQSKYAELLAIIEELGKEIRPTYAGSKSS\MERL\KRGIIHARGLVRECLAETERNARS
4488	34856	A	4529	1	653	MAGPAESSPQGAHPNSPFALQHHSSLTVKPLHRQNVIQHQVAGQENRRGHQAGSSTSPQPLEALKRPNLRAPFHSQSRRILIPPAGNPTPGAAAPADPSTQRRDRWGCALPMPRVAAGSAHHQQAGPTAAAQHRTPVALFSPPLSLVYGQQQRKESETPTVPTPPARARGWTETGVEHVPAYNRTRAPEKCDI/SVPSPHSSPDAETSHPRHISPCPG

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4489	34857	A	4530	3	432	NSRVDDFVAAQDAKGKKVAP APAVVKKQEAKKVVNPLFEKR PKNFGIGQ\QRLLARAEKKAAG KGDVPTKRPPVLRAGVNTVTT LVENKKAQLVVIAHDVDPIELV VFLPALCRKMGVPYCIIKGKAR LGRLVHRKTCTTVAFT
4490	34858	A	4531	1	2073	MKPCAHSWNAELSRNIIRHSFN LVMVAASQVAVSQLLGSYEILL LVSIELMFCFGLGYFFIPMQEW PNTYGERVFVDVESSVFKWNH KCLHKTEAERDYTKKRLKLCG HKPGNAVGQQKLEEARNRFFT RAPGGSAALPTLRFQPSDTDFR LLASRTILTFETKNPSELAERLR SVCGNQSNAYARLLEYRLNAL RGLWNAQRQLALEEQHERESS GDEETLALLKRQGLLQQPEQAP FTSRMGLLLVFPLIQSQSRTDPS LCNITAEVLLNCLRDCQPLSLT KEPADCLNGIETLLCSWLEETS DTGRHIPHKQKENAAAALVAL ACARGFVYCRNEELEPGWVAF GSGSLLHRPVSFDNKPHSLFQVI DQNTLQVCQVVPMPANHLPIG STMSTVHLSSDGTYFYWIWSPA SLNEKTPKGHSVFMDIFELVTL KGKKAKGKKVAPAPAVVKKQ EAKKVVNSLFEKR\DIQPKRELT YFVKW/PRYVRLQQQRAILYKQ LKVPPAINQFTQALNCQTVTQL LKLAHKYRPETKQEKKQRLLA QAEKKAAGKGGVPTKRPPALR AGVNTITTLVENKKAQLVVIAH DVDSIELVVFLPALCCKMGVPY CIIKGKARLGRLVHRKTCTTVA FTQVNLEDKGALAKLVEGIRTN DNDRYDEICCHWGGNILGPKS VACIAKLEKAKAKELATKLG
4491	34859	A	4532	1	2565	
4492	34860	A	4533	1	644	MPKGKKAKEKKVAPAPAVVK KQEAKKVVNPLFEKRPKNFGT GQDIQPKRDLTHFVKWPCYIRL QQQRTILYKWLKVPPEINQFTQ APDSQTATLLLKLAH/KYRPET NQEKKQRLLARAKKKAAGKG DIP\TKSPPVLRAGVNTITTLVE NKKAQLVVIAHDVDPIKLVVFL PVLCHK/MGVPYCIIKGKARLG HLVHRKTCTTVTFTQVNSEDK

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4493	34861	A	4534	1	931	KSIQKGLKMCLSSSLLPPSKMPKGKKAKGKKVAPAPAVVKKQEAKKVVNPLFEKRP\KNFGIGQDIQP\KRDFTRFVKWPRLLSGCMR\KRAILYKAG*KLPPA\INQFHPGPWDPANKLLQLL*AWAHK\YRP\ETKAKRKKQRL\LARA\EKKAA\GKGDVPNERDPPV\LRA\GVNTVTHLWWRNKKAPAWVVIATRRWIPFEL\VVFLPAL\CREKWGSPYCIIKGKARLGR\LVH\RRPCT\TVGFHTR*NSKDKRRLLA*AGLEAIRTQFTIDQIRWRSGRH\WG\GNVLG\PKSVARIRQASKRQRLKELATKLG
4494	34862	A	4535	3	227	
4495	34863	A	4536	1	338	
4496	34864	A	4537	1	352	
4497	34865	A	4538	2	368	
4498	34866	A	4539	3	468	
4499	34867	A	4540	2	790	PRGRNRRRKTFQERRMTLNESPEKIGKWIECYGHPPASKLVEIYIHTVFVEDKLSICIRSFNKKADGSWRMTVDYCKLNQVVTAIAAAIPDVVSLLEQINTSPDTWYAAIDLANALFSIPVHKGYINSLALCHNVIWRELDCFSLPRDTTLVHYIDDIMLIGSSVQEVENKLDLLVKDKLLHLAPPTTKEEVQHMVGLFGFWRQHIPHLGVLHQPIYRVIRKAA/SFEWGPEQEKALQQVQAAVGGKQSENNLGHQRSPGLW
4500	34868	B	4541	179	1219	
4501	34869	A	4542	1706	2517	THLLVPGMQPLTWQMPFSPFLSISPTRSNLPSAATPVIAQWA/HEQSGHGGRDGGYTWAQQHGLAFTNTDLATVNAKIGFAYPVCDASAKTTIRGLLECLIRCDGIPHSIASDQARIHRSRNQEVEVEVAPLTITPSDPLAKFLLSVPVTLRSAGLEVLVPGEGMLPPGNTRTIPLNWKLRLPPGHFGLLLTLSQEAKNGVTVLAGVIDLDYQDEISLLLHNGGKKEYARNTGDPLGRLLVLPCPVIKINGKLQQPNPGGTTNGSDPSGMKV

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4502	34870	A	4543	3	367	DLWPFTRVTVH/WGKANDQTF QGLLDTGSELTLIPGYPKRHCC PPVKVRVYGGQTDGSWRMTV GYHKLNQVVTPIAAAVPDVVS LLEQINTTPAIKWVVHSSIPSSN GSGVYVIRLEQVLKAQ
4503	34871	A	4544	2	541	
4504	34872	B	4545	1	681	
4505	34873	A	4546	2	1091	PRGRNRRRKTFQERRMTLNESP EKIGKWIECYGHPPASKLVEIYI HTVFVEDKLSICIRSFNKKADGS WRMTVDYCKLNQVVTAIAAAI PDVVSLLEQINTSPDTWYAAID LANALFSIPVHKGYINSLALCH NVIWRELDCFSLPRDTTLVHYI DDIMLIGSIKFLGVQWCGACRD IPSKDPADPMVLEVSVADRDAV WSIWQALIDESQQRPLGFWSKS LPSSADNYSPFERQLLAYYWAL VETERSTMGHQVTMLPELPVM NWVLSDPSSHK/ANGLAGWSG TGKKHDWKIGDKEIWRRGMW MDLSEWSK/D/VKIFVSHVSAH QRVTSAEEEFNNQVDRMTRSM DTTQPLYPTTPVIAQWAHE
4506	34874	A	4547	1	1236	
4507	34875	A	4548	1	1467	GEKGNDQTFRKLLDTGSELMLI PLRVVIPTTSLFNSPIWPVQKTD GSGRMRVDYHKLNQVMTPTA AAVPDVVSLFEPINTFLGTWYA AIDLANALFSIPVCKAHQKQFA FSWQGQQYTFTVLPQRYINCLA LCHNLIQRDLDHFLLPQGITLV HYIDSGPFIK*PEAASFEWGPEQ EKALQQVQAAVQAALSIGPYD PADPMVLEVSVADGDAVWSL WQAPKGESQWRPLGFWSKALP SSTDNYSSSDVQLYTDSWAVA SSLAG*SGTWKKHDWKIGDKEI WGRGMWMDLSEWSKTGKIFV SHVNAHQLVTSAEEDFNNQVD RMTRSVDTTQPLSPATPVVAQ WAHEQSGHGGRNEGYAWTQQ HGLPLTKADLTTATAECPICQQ QRPTLRPRYGTTSQGDQPATC WQVDYIEPLPSWKRQRFLLTGI NTHSGYGFAYPPCNASAKTTIH GLIACLIHCHGIPHSIASLYRER GTHFTDKEVQQWAHAH

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4508	34876	A	4549	2	1602	NLSPILPQDLWPFTRVTVHWGKGNDQTFQGLQDTGSELMLIPGDPKRHCSPPVKVGSYGGQVINGVLAQVRLTVGTVGPRTHPVVISPVPECIIDIDILNSWQNPHIDSLTGRVKAIMVGKAKWKPFEPLLPIKIVNQKQYRIPGGIAEISATIKDLKDAGVVIPITLPFNSPFWPVKKTDGSWRMKVVYCKLNQVVTPITAAVPDV/VVSLLEQINTSPGTWYAAIDLANAIFSIPVHKAHQKQFAFSWQGHQNTFTVFTILLHIHKVGHAQQHSIIKWKWYIHDGARAGSEGTSKLNEEVPQMPMVTTSAALPSLPRPAPMASWGVLYDQLTEEEKTRAWFTDGSARYAGTTQKWTAAALQPLSRTSLKGSGEGKSSQWAELQAVHLVVHFSWKDKWPDVRLYIDSWAVANGLAGWSGTWKKHDWKIGDKEIWGRGMWMDLSEWPKPVKIFGSHVSAHQWVISAEEDFNNQVDKMTCSVDITQPLSPATPVITQWAHKQSGHGGRDGGYTWAQQHGLPLTKTGLAMATAECPI

SEQ ID NO:	SEQ ID NO: of peptide sequence	Met hod	SEQ ID NO: in USSN 09/540,217	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown, *=Stop codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
4509	34877	A	4550	1	1891	MLSSTQNAGGSYQRVRGALDTQEWKWGEVSPRTLNVDGRALVSVANTHGTDRPAYTLNPQSRDQRSGVITLGYKRPLEREDLFELKESDSFCTACPIFEKQWRKEVLRNQERQKVKALNKLDEALCPGIILTQSTDSNANLFQKQPHRHTQTSGRWQIIIFCEHSSDFGWNGYGYAVALLVVVFLQTLILQQYQRFNMLTSAKVKTAVNGLIYKKLGWSGKVSWLILHDVGHGIMEGYIAWGKGSDVRITWEKKSTEMRTRPAQKMALLLSNVSRQKFSTGEIINLMSATHGLDSKPQSPLVCPFSNPNGRISPLARAGLADHYRVTHLQILKLYAWEPSYKNKIIKIRDQELEFQKSARYLTVFSMLTLTCIPFLTKISLGRLEDFLNTEELLPQSIETNYTGDHAIGFTDASFSWDKTGMPVLKESIRIRIEQVLNQLSLFETVDYPGSVAYVSQQAWIQNCILQENILFGSIMKKEFYEQVLEACALLPDLEQLPKGDQTEIGERAVNISGGQQHRVSLARAVYSGADVYLLDDPLSAIDVHVGKQLFEKVIGSLGLLKNRTHILVTHNLTLLPQMNLIVVMKSGRIAQMGIYQELLCKTKNLTN\FTKSSVNKKKVGEWEESGRGS
4510	34878	A	4551	2	542	LTSAKVKTAVNGLIYKKVSLATLCVYFLLDERIILTAPKVFTSMSLFNILRIPLFELPSVISAVVQTKISLGRLEDFLNTEELLPQSIETNYTGDHAIGFTDASFSWDKTGMPVL/NRGSEAYVSQQAWIQNCILQENILFGSIMKKEFYEQVLEACALLPDLEQLPKGDQTEIGERVR
4511	34879	A	4552	1	667	IETNYTGDHAIGFTDASFSWDKTGMPVLKESSVAYVSQQAWIQNCILQENILFGSIMKKEFYEQVLEACALLPDLEQLPKGDQTEIGER/GKETAVNISGGQQHRVSLARAVYSGADVYLLDDPLSAIDVHVGKQLFEKVIGSLGLLKNRTSHSVCHYTLLAVPHLLEVQILTGNFIQSLGFNYHEYANNSNAYIVNLDLFPGFQTCVYKLLSPIRCLIC
4512	34880	A	4553	201	336	QQTPGKAVHAPFIADQSLT*ELVSVFPQFQLFPYRR*DSHSGKS
4513	34881	A	4554	3	515	

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4514	34882	A	4555	1	852	MPCTTSGLDKVPTSKKALTRYGYGSLTLDFSGSIIPCKMCLSPSTRIVRPSQPRGTEDPDETGDTEFVNSDESFLLEGTASPSPVVAVSPPRPMLPSAFPPLSEDINPVLPEATVLASPEVVAKQTHVDSPRKPLSTFLFASRPVTKLKSRQTPGGEVDSVTCEEKTDGPWRKTVDYCKLNQVVTPIAALVPDMVSLLVQINTSSDTSYAAIDLAKAFFSIPVYKAHQKQFIFSWQAQQYTFTVLPQGYIISPALCHNLIRR/DLDHFLLPQDITLVHYIDDIRL
4515	34883	B	4556	288	327	
4516	34884	A	4557	51	598	LFGGCHTSGGLAVRVPRMPRGSRSRTSRMAPS\ASRAPLK*ELEPRQAQVAQPPA\AAPPSAVGSS\AAAPRQPG/LFMAQMATTAAGVA\\VGFCCGGHTLGHGI\TGGLSVGGKLIA*ALRRP*HQFNQGSFRGTQAKHSKQQPALPLLWRIKTSFREVVPPEPRVTIQGFCGGFPMRLLETVPDL
4517	34885	A	4558	1	10434	MTVIRSGIAYILHLKSYDVNIQTGSNACNQPTHPNGDCSHFCFPVPNFQRVCGCPYGMRLASNHLTCEGDPTNEPPTEQCGLFSFPCKNGRCVPNYYLCDGVDDCHDNSDEQLCGTLNNTCSSSAFTCGHGECIPAHWRCDKRNDCVDGSDEHNCPTHAPASCLDTQYTCDNHQCISKNWVCDTDNDCGDGSDEKNCILNCTASQFKCASGDKCIGVTNRCDGVFDCSDNSDEAGCPTRPPGMCHSDEFQCQEDG
4518	34886	A	4559	24	849	ATGRCCCGLAPGFPLCWVLYPGGRGSA\CPEPHVLRTGSPLQREQRTNGRTDLSSLLPNLNFDSPPRCKHKNQLAITLRKRIRKLATSLFSSTIFRISGTSVIISAPGAGLPLPALFPTRCQPKFSRSIDPTGKAVQTADIRLSARATLWLGGSIEESPVLCSTLRLLLRRLPPPLTWTSPNRPTQPCTAQTQTNQSVGIAAPSAIRVIYPESVVLNAVIYLPGDPEVSGLPRAFKRRFSVEVRLDCGTFKLLLVYCTHPGDKKVNTCKTGALVAF
4519	34887	C	4560	192	449	
4520	34888	A	4561	1	786	
4521	34889	A	4562	3	14073	

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4522	34890	B	4563	58	1282	
4523	34891	B	4564	1	684	
4524	34892	A	4565	1	1356	MGRKYTLKWEFEEGFTEKKEL KKVTSEGYITPVEIYDYRQYCY ALQRPIATTQIDDVRDGHTTRL AKLEKQEQTHSKASRRQEIIKIR AEPKEIETQKTLQKINESRSWFF EKINKIDRLLARLIKKKREKNQI DAIKNDKGDITTNPTEIQTTIRE YYKHLYANKLENLEEMDKFLH TYILPRLNQEEVESLNRPITGSEI EAIINSLPTKKSPGPDGFTADFY Q\MLEVLARAIMQEKEIKGIQL GKEEVKLSLFADYMIVYLENAI ISAQNLLKLI/SNFSKVSGYKINV QKSQAFLYINNRQTESQIMSER PFTIASKRIKYLGIQLTRDVKNL FKENYKPLLNEIKEDTNKWKKI PCSWVGRINIVKMAILPKVIYRF NAIPIKLPMTFFTELEKTTLKFI WNQKRACITKSILSQKNKAGGI MLPEFKLY/YQGSSTQTAWYW
4525	34893	A	4566	1	1102	MANCDINRKDEKGGKEKKDRS KSKSLMDTLKRQLSAKQKPKG KAGKPSGSSADEDTFSSSSAPIV FKAVRAQRPIR/STSLRSHHCSP MPWPLRPTNSEETCIKME\PSPP LNGVRKDFHDLQSETACQEQA NSLKSSASQNGDLYLRLDEHVP VVIGLLPQDYIQYTVPLDEGMC PLEGSSSYCLDSSSTMEVSVVPS QVGGRSFPEDESQADQNLVVA PEIFVDQSMNGLLTGTTGVMLQ SPRVGPHHVPPLSPLLPPMQNN QIQRNFSGLTGTEAHMAESMLC HLNFDFNSAPGVARVYVSVQSS GPMVVTSLTEELKR\LAKQGWL WPPLKSVRRCVLARRSLYTKQL NQEEGTELNLGSSCLLC
4526	34894	A	4567	364	661	PFHFTCFSCKVYFADPGSAARS VPGSPSAVCAQCILCTGHCAVC PGLGEHHSSGRTLMKTKLHSK KLKPCYLLC*SKN*KTQGGSPK S*NVNKYLVTLI
4527	34895	A	4568	53	470	CISIIILPGPSAKTLSPVLSLSSPY TASFQPTFVRTFSHQTTYLSLGS VPVAQLKCSAGQQRGELLCRR GVWGSWISVSHFTEIATLPAAC LEDGE\DFNLGGILDSSKYL*SIQ KTNTHRIVDGKVVSETNITDVL

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4528	34896	A	4569	1	1635	MGWTCKILFLVAAATGAHFLVQLVQSGAEVKKPGASVKVSCKASGYTFTYCYLHWREPVSFICGRCILLTLLLGDCLWGEGAWTQGDVLQPSDRASFLAMGVNTTGQQVGDLSGDFPNSVGKACKCREFHTLTPLAHTSSTTHETFPGMSHIALELSQGSSLLQCLEAQTQGQRQELTVSANEQPESRGHGCVLLCETQSEGKSVRAQAQTSLKGSQKRLGGARTLCTGLSPGQRKQERSKIDTLTSQLKELEKQEQTYSKASRRQEITKIRAELKEIETQKTLQKINESRSWFFEKIYKIDRPLARLIKKKREKNQIDAIKNGKGDITTDPTEIQTTLRQYYKHLYANKLENLEGMDKFLDAYTLPRLNQEEVESLNRPITGPEIEAIIN/STPTKKSPGPDRFTAEFYQ\RSDVLARAIRQKKEIKCIQLGKEEVKLSLFADDMIVYLEIPIISAQNLLKLISNFSKVSGYKISVQKSQAFLYTNNRQTESQIMSELPFTIASKRIKYLGIQLTKDVKDLFKDNCKPLLNEIKEDTNKWKNIPCS
4529	34897	B	4570	1	429	
4530	34898	A	4571	1	897	MDLNYTLEQMDLTDIYRTFHPTTTEYTFYSTGHGTFSKTDDVIGHKMSLDKFKKIEMISNTVSDHSGIKLEINSERNLENHANTWKLNNLLLNECWVKNKMKMEIKKLFELNDNNDTTYHNLWDRAKVVIRGKCIALNTYIKKSERAQTDNLRIKNKNHMIISIDAEKAFDKIQHPFMIKTLSKISIRGTYLNLIKDIYDKPTANIMLNGEKLKAFTLRTGT\RMNQGCPLPSLLFNI/VLEVLARAIRQEKEIKGIQIGKEEVKVSLFADYVIVYFENPTDSSRKLLELIKEFSSFWIQD
4531	34899	A	4572	1	1461	
4532	34900	A	4573	49	365	
4533	34901	A	4574	45	534	VCHLEPGERCGPSRGCRAVGVQTEKMQTAGALFISPALIRCCTRGLIRPVSASFLNSPVNSSKQPSYSNFPLQVARREFQTSVVSRDIDTAAKFIG\AGSATVGVADSGAGIGAVFGSLIIVYARKLSLKQQLLFYAILGF\ALSEGM\GLFCLMVAFLILFAM

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4534	34902	A	4575	98	624	DWYSRSHPKELWEGSKKKSINHSACSLQAHGGPISTSLNPHSKPRGRVSPPPGKRQQECRARPGRSPELAGPPPANVQETSQKNACASRLSEPPGEGP\EPAAHPQPHRGSSSGPCSRGGYRQPLFPGPAASGVPASGSV/RSRIPGAPQGVALARRGPQGSPSPAPRFFPATERQS
4535	34903	B	4576	1	604	
4536	34904	A	4577	3	331	LAPAPSAAWRTGLKALTPSSTWMLCASE\HHVGSGCVGDHLAGCRQEKTLPCQR\YCVFCRRRRARSLQAQCGFSLTPALELLPVPFLKLLCPGPPRRRRICRILPGAGL
4537	34905	A	4578	1	871	
4538	34906	A	4579	3	510	GPPSRVDDFVAAAAAAVAPVVLYACPRHSPIPPWSIRGRRVVVTGFGPFGEHTVNANWIAVQELEKLGLGDSVDLHVYEIPVEYQTVQRLIPALWEKHSPQL\VVHVGVSGMATTVTLEKCGHNKGYKGLDNCRFCPGSQCCVEDGPESIDSIIDMDAVCKRVTTLGQCI
4539	34907	A	4580	1	285	MAPGALPALGEEEGPGASGLSAELGHLSAGSRAFRETSVDSALDTPFPAGTFVRLEFKLRQTE\SGRRKDWKKPKCKVQPERRKQKCLTCVKLEC
4540	34908	B	4581	1	228	
4541	34909	A	4582	1	697	MGLERPVDRVMWLPGALWNSAVVSAPVGEEWALAGTGNQGLQDIQGMHCPEEGISQIHGRDHRNAKDSHTGVWCSCTLGIISTIIIRPKCRFSIDRSDSDYLPTSSCRRDPGGAEPCQDRPRVEQLCSVLANRSGPLAKCHWYESPVSYTQVCVSDLCQYGTGNRMLCTMLEAYVQLCALRCALPARVASQPGMQLRVACPANSYYDSCGPPFPATCASLNSSAPCTLQCTVSCFCLEGFALEAG\SSVPHACCGCHLQGRYI/APGPWPSATGMRAPCPTRRCVSLTSASMARATACCAPCWRPTSNSAPCAARCLPAWRASLGCSYVWRVQPTATMTPVGHPSRPPVLASTPPRPAPSSAQ
4542	34910	B	4583	1	208	
4543	34911	A	4584	2	230	

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4544	34912	A	4585	106	669	GCGCVLLPGGVGAPGHSPEGPVPPRDARQLRTCGLAGTLHLSTSCGHPTGAWRGALGSQWNGHNPVQDHLQEAQPWFLEFDRG*RCFWRMATSFPRYPTWDDY*RLPCCRCLPQCKKPAETTGCLPISGEKTHGGVGDLLGEAPARLRQWASQRQPATDLPA*ASRGRPA*GKDTHRACVAGEAAQDA
4545	34913	A	4586	2	597	TPKGGIRLGLAKLGCPTAWINPYGRGMPLAHSVLSSGARVLVVDPDLRESLEEILPKLQAENIRCFYLSHTSPTPGVGALGAALDAAPSHPVPADLRAGITWRSPALFIYTSGTTGLPKPAILTHERVLQMSKMLALSGATADDVV\YTEVLPLYHVMGLVVGILGCLDLGTSLASYGLRVYFILWSVLGPSRRTLCL
4546	34914	A	4587	9	573	EEEERKKKKK\KKKEEEEGEEEGGGMGEKKKKEEEEEGEEEGEKEREKER\EKERKKKKEERKEKERERKKKRERKKEKERERKEGEGERERKSTECTSSSYI/IKKLVVKQPQAAPSGEIPEEGIAVLGGDSSMPVIVPEDLPVGQDVEVEDSDINDPDSLILVSSQAGGGGVITAYCNLEHLGSSDPPT
4547	34915	A	4588	1	297	
4548	34916	A	4589	114	752	DGSAAPRATSDSFTYTVCVSEFPVDDFMELGRSIPDTQL/DAVIESQKANQCAVLIYT/SGTTGIPKGVMLSHDNITWIAGAVTKDFK/PTDKHETVVSYLPLSHI/AAQMMDIWVPIKIGAL/IYFAQADALKVRLSKDLGSDFILLGSPVGLRPSTKRLPVLSKLGHTYRRVVWVEESSGPHTISNQNNYRLQGPMMKLKRHFVAQKYKKQIDHMYH
4549	34917	A	4590	1	837	MVTQKLPNAQENLKHAERQAAGCCPGRSHIFQHVGPGASESLRGEGCSTHPEAQGAQERCEQWKKDQHWCLASHTDVTQQWGRHIVQEGGTHRGPSAVLSLRTALDEG/ARGGCSHPITAQLPLQLRHLPRPPPAPAR\PSPAPPAATSPPT\PPPAPAR\SSPAPPAATSPPTASSGACAALPQLPLQLRHLPRPPPAPAR\SSPAPPAAMSPP\RPPAPARPRLRRSTACATALRPGERGSAAAQPGARSETSFCRLG/AAAAVLDPAFISSQALACPVVGVI

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4550	34918	A	4591	3	377	
4551	34919	B	4592	1	1632	
4552	34920	A	4593	1	1224	MDGTNRFYLYVWETERQQDV EHVARCILCYDKCRPDPECPAG TPGPQEVDVDLVFVVDSSYGV DADVYRGSLSLADAALEDLEV AEQPGASHRGARVALVTHTTP NF\GRGFHLTTYGNRKQMQRH VREASARPLQGTAPPGHALEW TLENVLLAAPRPRKAQVLFAIV ASETSSWDREKLWTLSLEAKC KGITLFVLALGPGVGTHELAEL AELVSAPSEQHLLRLQGVSEPE VNYAQGFTRAFLNLLKSEQSPG TGAPWVEWGEGFTEPGIWACR WTNQYPPPELTEECGGLHRGD TVLQLVTPVNRFMYAAKENSL KRKTKANFHLAVELELDESYFR AYYEGTLYEVSALPLQRSNELL QKWSLFHGSNGRRVSGSHPEV ALQQGGTGLPAVLVWQLWRQ
4553	34921	A	4594	266	556	HKVQQICYRLRLVSQILFSINQT LAERQIVTFTVYPDTERDRETR NLADLKQIKIDLGKFSDNPDGY IDILRGLRQSFDLTW\RDIMLLL NQTLAPN
4554	34922	B	4595	1	735	
4555	34923	A	4596	70	624	PTAMVEEGIAAGGVMDVNTAV QEVLKTALIHDGLARGIREAAK ALDKYVYQSQYCGFLQPDQKL ATQGKKGMGVHGVKRKSS*M ASVLPGNLRKRRQAH\LCVLAS NCDEPMYVKLVEALCAEHQIN LIKVDDNKKLGEWVGL\CKIDR EGKPRKVVGCSCVVVKDYGKE SQAKDVIEEYFKCKK
4556	34924	A	4597	145	682	SWRNRTVSNGSAVSASSVHLCF AECKALCGERILTDGSDVSRPTI AAGGVTDVNTALQEV\LKTALI HDGLAR\GISRTWPKAL\DKRQ AH\LCVLASNC\DEPMYV\KL\V EALCAEHQINLI\KV\DDNQET* EKWV\GLCKI\DREG\KPRE*WL VGS*CSSLRTIGKESQAKDVIEE YFKCKK
4557	34925	A	4598	252	590	RSLDLVWWQLSGGLAGSAKPK PCTPVKQSTVMSFPSHKEQYFL MDGKKK/YDKESEKYYSILEKH LNLSAKKKESHLQENSSGPSVS TKLINLFSKRLLCAFLPAQLTPY SFCS

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4558	34926	A	4599	1	1662	
4559	34927	A	4600	4430	4904	LIKGTRCLGRRPSFAYSRSNI*A *S*P/EGTSAQLAELLALTLALE LGNGKRINVYTDSKYAYLILHD HAAIWKERAFLTSGGTPIKYHK EIMELLHTVQKPKEVAVLHCQS HQKESSPLEDTTTAGPLLHPYP AGSSPERSSPSSQQLLGDLFRGII
4560	34928	A	4601	1	2630	MEQANHPVRLINVVCKDTLKKI VQQETSCPLTHVHYAEAITGRC TAPEDKGSLDQKPPTDDPTGCP WQVPAHVITLTETWVCLTIEGQ EIDFLLDTGVQKPNGQWRLVQ DLIPIKEAVIPLYPVVPNPYTLIS QIPEKAEWFMALDLKDAFFCIS LHSDSQFLFAFEDPTNHTSKITR TVLPQGFRDSPPLFGQALAQDL GHFSSPGTLVFQYVDDLILATSS EASCQQATLDLLNFLANQGKV VPNLWGKLPLNTTRKSWSYCT QCKNPRRWQSYTAKAIKKQLA EAGPVTAILLLLIFGPCIFNLLIK FVSSRIEAIMLQMVLQMEPQMS STNNFYQGPLDRCTDPLSGLES SPRCSEAPCLMSQWTGDIEYDL LLPPIPHQTTLCDLQNLKGIFSR YHRKWYGEILALLTPTANVCG HSQVPHACSIYHDPVTWNPQG LLPKSLYGVTKWGDKEHFEWG SQQQRAFYELK\KKLMSAPALG LPDLTKLFTLHVSDREKKMAV RVLTQTMGPWLGPVAYLSKQL DGVSKSWPPCLRALAATALLA REVDKLTLGQNLNIKAPHAVV TLMNTKGHHWLMNARITRYQS LLCDKPHITIEVCNTLNPTTLLL VSESPVEHNCVEVLDSVYSSRP NLRDHPWTSVDWELYVDGSSF INPQGESVWGIIQGKRPIKLWG KRRKVSARDLAIIGGSVEAPKL
4561	34929	A	4602	1	506	FLALTSRFLFVLLNEETRSHLEK SLCWKVSPHIKMDLLQWIQSK AQSDGSTLQQGSLEFFSCLYEIQ EEEFIQQALSHFQVIVVSNIASK MEHMV\SSFCLKRCRSAQVLHL YGATYSADGEDRARCSAGAHT LLVQLPERTVLLDAYSEHLAAA LCTNPNLIELSLYR
4562	34930	A	4603	3	381	
4563	34931	A	4604	3	483	
4564	34932	A	4605	3	410	

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4565	34933	A	4606	2	249	SADAPMFDMGVNHEKYDNSLNII/SVMKAGPVEKRPAWHPMDTLP*LAPRSLFLCSNASCTTNCLEPLAKVIHDNFGIVEGLMV
4566	34934	A	4607	2	481	LAPLVKEIHDNFGMGEGLMTTGHAITATHKTADGPSGKLWRD\GRGAHQNIIPASTGAAKAVGKVMPELNGKLTGVAFRVPTANVSVVDLTCRRQKPAKYDDIGKVVRQAPEGPLKGILGYTEHQVVSSDFNSDTHSSTFDAGAGIALNDHFATLSPPPH
4567	34935	B	4608	79	278	
4568	34936	A	4609	2	1201	PSTACRNSARACSTVSRIFFCVASRATSLRTPMGKVKVGVNGFGRIGRLVTRAAFNSGKVDIVAINDPFIDLNYMVYMFQYDSTHGKFHGTVKAENGKLVINGNPITIFQER\YPSKINWG\DAGAEYVLESTGAFTTMENAGAHLQGGAKRVIISAPSA\D\APMFVMGVNHEKYDNSLKIISNA\SCTTNCL\APL\AKVIHDNFG\IV\EGLMTTVH\AIT\ATQKTV\DGPSGK\LWALMGPRGFFQEHQSLPFTGGC/ARVVGQGSSPELERGKLTWAWAFRCPQLPKRVNGWDL\TCRL\EKPCPKYD*HQGRVVKAGRRKGPLQGAILGLQLSNPGGSPSGLSTSDNPLLPPFDAWGLAFALQRTHFCSKLIFLGIDNGILGYSNQGGWDLHGPPWPTWAFQGS
4569	34937	A	4610	61	226	WRIMPTKKVMITMGRTTQRRMLES/SQQFWPCHLH*KLVPSCLQLGCLVFHFRRER
4570	34938	A	4611	153	495	QHAAECKAHAGLPGLPLPARKLASRHGAPRWRQSGVGPGGKVENYGRRRL\PGTRHPQSLSHKPAKKIDVARVTFDLYKLNPQDFIGCLNMKATFYDTYSLSYDLHCCGAKRIMK
4571	34939	A	4612	1	643	
4572	34940	A	4613	286	698	ESDNNLTQGTSI*QGTRHPQSLFPLSPAKKI*CGPVLTFLTCYKLNPQGLSLGCLNIEGRFFMDYVIPFPIDLALLLGAKRIMKG\TLHWALFSMQTTGPRA/VFTSCYLQQLLDATEDGHPPKGKASSLIPTCLKILQ
4573	34941	A	4614	59	294	
4574	34942	A	4615	1	2253	